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(57) Abstract

Isolated polynucleotides encoding polypeptides expressed in mammalian skin cells are provided, together with expression vectors and host cells comprising such isolated polynucleotides. Methods for the use of such polynucleotides and polypeptides are also provided.

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POLYNUCLEOTIDES ISOLATED FROM SKIN CELLS AND METHODS FOR THEIR USE

Technical Field of the Invention

This invention relates to polynucleotides encoding polypeptides, polypeptides expressed in skin cells, and their use in therapeutic methods.

Background of the Invention

The skin is the largest organ in the body and serves as a protective cover. The loss of skin, as occurs in a badly burned person, may lead to death owing to the absence of a barrier against infection by external microbial organisms, as well as loss of body temperature and body fluids.

Skin tissue is composed of several layers. The outermost layer is the epidermis which is supported by a basement membrane and overlies the dermis. Beneath the dermis is loose connective tissue and fascia which cover muscles or bony tissue. The skin is a self-renewing tissue in that cells are constantly being formed and shed. The deepest cells of the epidermis are the basal cells, which are enriched in cells capable of replication. Such replicating cells are called progenitor or stem cells. Replicating cells in turn give rise to daughter cells called 'transit amplifying cells'. These cells undergo differentiation and maturation into keratinocytes (mature skin cells) as they move from the basal layer to the more superficial layers of the epidermis. In the process, keratinocytes become cornified and are ultimately shed from the skin surface. Other cells in the epidermis include melanocytes which synthesize melanin, the pigment responsible for protection against sunlight. The Langerhans cell also resides in the epidermis and functions as a cell which processes foreign proteins for presentation to the immune system.

The dermis contains nerves, blood and lymphatic vessels, fibrous and fatty tissue. Within the dermis are fibroblasts, macrophages and mast cells. Both the epidermis and dermis are penetrated by sweat, or sebaceous, glands and hair follicles. Each strand of

hair is derived from a hair follicle. When hair is plucked out, the hair re-grows from epithelial cells directed by the dermal papillae of the hair follicle.

When the skin surface is breached, for example in a wound, the stem cells proliferate and daughter keratinocytes migrate across the wound to reseal the tissues. The skin cells therefore possess genes activated in response to trauma. The products of these genes include several growth factors, such as epidermal growth factor, which mediate the proliferation of skin cells. The genes that are activated in the skin, and the protein products of such genes, may be developed as agents for the treatment of skin wounds. Additional growth factors derived from skin cells may also influence growth of other cell types. As skin cancers are a disorder of the growth of skin cells, proteins derived from skin that regulate cellular growth may be developed as agents for the treatment of skin cancers. Skin derived proteins that regulate the production of melanin may be useful as agents which protect skin against unwanted effects of sunlight.

Keratinocytes are known to secrete cytokines and express various cell surface proteins. Cytokines and cell surface molecules are proteins which play an important role in the inflammatory response against infection and also in autoimmune diseases affecting the skin. Genes and their protein products that are expressed by skin cells may thus be developed into agents for the treatment of inflammatory disorders affecting the skin.

Hair is an important part of a person's individuality. Disorders of the skin may lead to hair loss. Alopecia areata is a disease characterized by the patchy loss of hair over the scalp. Total baldness is a side effect of drug treatment for cancer. The growth and development of hair are mediated by the effects of genes expressed in skin and dermal papillae. Such genes and their protein products may be usefully developed into agents for the treatment of disorders of the hair follicle.

New treatments are required to hasten the healing of skin wounds, to prevent the loss of hair, enhance the re-growth of hair or removal of hair, and to treat autoimmune and inflammatory skin diseases more effectively and without adverse effects. More effective treatments of skin cancers are also required. There thus remains a need in the art for the identification and isolation of genes encoding proteins expressed in the skin, for use in the development of therapeutic agents for the treatment of disorders including those associated with skin.

Summary of the Invention

The present invention provides polypeptides expressed in skin cells, together with polynucleotides encoding such polypeptides, expression vectors and host cells comprising such polynucleotides, and methods for their use.

In specific embodiments, isolated polynucleotides are provided that comprise a DNA sequence selected from the group consisting of: (a) sequences recited in SEQ ID NO: 1-14, 45-48, 64-68, 77-89, 118, 119, 198-231, 239-249, 254-274, 349-372 and 399-405; (b) complements of the sequences recited in SEQ ID NO: 1-14, 45-48, 64-68, 77-89, 118, 119, 198-231, 239-249, 254-274, 349-372 and 399-405; (c) reverse complements of the sequences recited in SEQ ID NO: 1-14, 45-48, 64-68, 77-89, 118, 119, 198-231, 239-249, 254-274, 349-372 and 399-405; (d) reverse sequences of the sequences recited in SEQ ID NO: 1-14, 45-48, 64-68, 77-89, 118, 119, 198-231, 239-249, 254-274, 349-372 and 399-405; (e) sequences having a 99% probability of being the same as a sequence of (a)-(d); and (f) sequences having at least 50%, 75% or 90% identity to a sequence of (a)-(d).

In further embodiments, the present invention provides isolated polypeptides comprising an amino acid sequence selected from the group consisting of: (a) sequences provided in SEQ ID NO: 120-197, 275-348, 373-398 and 406-409; and (b) sequences having at least 50%, 75% or 90% identity to a sequence provided in SEQ ID NO: 120-197, 275-348, 373-398 and 406-409, together with isolated polynucleotides encoding such polypeptides. Isolated polypeptides which comprise at least a functional portion of a polypeptide comprising an amino acid sequence selected from the group consisting of: (a) sequences provided in SEQ ID NO: 120-197, 275-348, 373-398 and 406-409; and (b) sequences having 50%, 75% or 90% identity to a sequence of SEQ ID NO: 120-197, 275-348, 373-398 and 406-409 are also provided.

In related embodiments, the present invention provides expression vectors comprising the above polynucleotides, together with host cells transformed with such vectors.

In a further aspect, the present invention provides a method of stimulating keratinocyte growth and motility, inhibiting the growth of epithelial-derived cancer cells,

inhibiting angiogenesis and vascularization of tumors, or modulating the growth of blood vessels in a subject, comprising administering to the subject a composition comprising an isolated polypeptide, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of: (a) sequences provided in SEQ ID NO: 187, 196, 342, 343, 395, 397, and 398; and (b) sequences having at least 50%, 75% or 90% identity to a sequence provided in SEQ ID NO: 187, 196, 342, 343, 395, 397, and 398.

Methods for modulating skin inflammation in a subject are also provided, the methods comprising administering to the subject a composition comprising an isolated polypeptide, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of: (a) sequences provided in SEQ ID NO: 338 and 347; and (b) sequences having at least 50%, 75% or 90% identity to a sequence provided in SEQ ID NO: 338 and 347. In an additional aspect, the present invention provides methods for stimulating the growth of epithelial cells in a subject. Such methods comprise administering to the subject a composition comprising an isolated polypeptide including an amino acid sequence selected from the group consisting of: (a) sequences provided in SEQ ID NO: 129 and 348; and (b) sequences having at least 50%, 75% or 90% identity to a sequence provided in SEQ ID NO: 129 and 348. In yet a further aspect, methods for inhibiting the binding of HIV-1 to leukocytes, for the treatment of an inflammatory disease or for the treatment of cancer in a subject are provided, the methods comprising administering to the subject a composition comprising an isolated polypeptide including an amino acid sequence selected from the group consisting of: (a) sequences provided in SEQ ID NO: 340, 344, 345 and 346; and (b) sequences having at least 50%, 75% or 90% identity to a sequence provided in SEQ ID NO: 340, 344, 345 and 346.

As detailed below, the isolated polynucleotides and polypeptides of the present invention may be usefully employed in the preparation of therapeutic agents for the treatment of skin disorders.

The above-mentioned and additional features of the present invention, together with the manner of obtaining them, will be best understood by reference to the following more detailed description. All references disclosed herein are hereby incorporated herein by reference in their entirety as if each was incorporated individually.

Brief Description of the Drawings

Fig. 1 shows the results of a Northern analysis of the distribution of huTR1 mRNA in human tissues. Key: He, Heart; Br, Brain; Pl, Placenta; Lu, Lung; Li, Liver; SM, Skeletal muscle; Ki, Kidney; Sp, Spleen; Th, Thymus; Pr, Prostate; Ov, Ovary.

Fig. 2 shows the results of a MAP kinase assay of muTR1a and huTR1a. MuTR1a (500ng/ml), huTR1a (100ng/ml) or LPS (3pg/ml) were added as described in the text.

Fig. 3 shows the stimulation of growth of neonatal foreskin keratinocytes by muTR1a.

Fig. 4 shows the stimulation of growth of the transformed human keratinocyte cell line HaCaT by muTR1a and huTR1a.

Fig. 5 shows the inhibition of growth of the human epidermal carcinoma cell line A431 by muTR1a and huTR1a.

Fig. 6 shows the inhibition of IL-2 induced growth of concanavalin A-stimulated murine splenocytes by KS2a.

Fig. 7 shows the stimulation of growth of rat intestinal epithelial cells (IEC-18) by a combination of KS3a plus apo-transferrin.

Fig. 8 illustrates the oxidative burst effect of TR-1 (100 ng/ml), muKS1 (100 ng/ml), SDF1α (100 ng/ml), and fMLP (10 μM) on human PBMC.

Figure 9 shows the chemotactic effect of muKS1 and SDF-1α on THP-1 cells.

Figure 10 shows the induction of cellular infiltrate in C3H/HeJ mice after intraperitoneal injections with muKS1 (50 μg), GV14B (50 μg) and PBS.

Figure 11 demonstrates the induction of phosphorylation of ERK1 and ERK2 in CV1/EBNA and HeLa cell lines by huTR1a.

Figure 12 shows the huTR1 mRNA expression in HeLa cells after stimulation by muTR1, huTR1, huTGFα and PBS (100 ng/ml each).

Figure 13 shows activation of the SRE by muTR1a in PC-12 (Fig. 13a) and HaCaT (Fig. 13b) cells.

Figure 14 shows the inhibition of huTR1a mediated growth on HaCaT cells by an antibody to the EGF receptor.

Detailed Description of the Invention

In one aspect, the present invention provides polynucleotides that were isolated from mammalian skin cells. As used herein, the term "polynucleotide" means a single or double-stranded polymer of deoxyribonucleotide or ribonucleotide bases and includes DNA and RNA molecules, both sense and anti-sense strands. The term comprehends cDNA, genomic DNA, recombinant DNA and wholly or partially synthesized nucleic acid molecules. A polynucleotide may consist of an entire gene, or a portion thereof. A gene is a DNA sequence that codes for a functional protein or RNA molecule. Operable anti-sense polynucleotides may comprise a fragment of the corresponding polynucleotide, and the definition of "polynucleotide" therefore includes all operable anti-sense fragments. Anti-sense polynucleotides and techniques involving anti-sense polynucleotides are well known in the art and are described, for example, in Robinson-Benion et al., "Anti-sense Techniques," *Methods in Enzymol.* 254(23):363-375, 1995; and Kawasaki et al., *Artific. Organs* 20 (8):836-848, 1996.

Identification of genomic DNA and heterologous species DNAs can be accomplished by standard DNA/DNA hybridization techniques, under appropriately stringent conditions, using all or part of a cDNA sequence as a probe to screen an appropriate library. Alternatively, PCR techniques using oligonucleotide primers that are designed based on known genomic DNA, cDNA and protein sequences can be used to amplify and identify genomic and cDNA sequences. Synthetic DNAs corresponding to the identified sequences and variants may be produced by conventional synthesis methods. All the polynucleotides provided by the present invention are isolated and purified, as those terms are commonly used in the art.

In specific embodiments, the polynucleotides of the present invention comprise a DNA sequence selected from the group consisting of sequences provided in SEQ ID NO: 1-119, 198-274, 349-372 and 399-405, and variants of the sequences of SEQ ID NO: 1-119, 198-274, 349-372 and 399-405. Polynucleotides that comprise complements of such DNA sequences, reverse complements of such DNA sequences, or reverse

sequences of such DNA sequences, together with variants of such sequences, are also provided.

The definition of the terms "complement," "reverse complement," and "reverse sequence," as used herein, is best illustrated by the following example. For the sequence 5' AGGACC 3', the complement, reverse complement, and reverse sequence are as follows:

complement	3' TCCTGG 5'
reverse complement	3' GGTCCT 5'
reverse sequence	5' CCAGGA 3'.

In another aspect, the present invention provides isolated polypeptides encoded, or partially encoded, by the above polynucleotides. As used herein, the term "polypeptide" encompasses amino acid chains of any length, including full length proteins, wherein the amino acid residues are linked by covalent peptide bonds. The term "polypeptide encoded by a polynucleotide" as used herein, includes polypeptides encoded by a polynucleotide which comprises a partial isolated DNA sequence provided herein. In specific embodiments, the inventive polypeptides comprise an amino acid sequence selected from the group consisting of sequences provided in SEQ ID NO: 120-197, 275-348, 373-398 and 406-409, as well as variants of such sequences.

Polypeptides of the present invention may be produced recombinantly by inserting a DNA sequence that encodes the polypeptide into an expression vector and expressing the polypeptide in an appropriate host. Any of a variety of expression vectors known to those of ordinary skill in the art may be employed. Expression may be achieved in any appropriate host cell that has been transformed or transfected with an expression vector containing a DNA molecule that encodes a recombinant polypeptide. Suitable host cells include prokaryotes, yeast, and higher eukaryotic cells. Preferably, the host cells employed are *E. coli*, insect, yeast, or a mammalian cell line such as COS or CHO. The DNA sequences expressed in this manner may encode naturally occurring polypeptides, portions of naturally occurring polypeptides, or other variants thereof.

In a related aspect, polypeptides are provided that comprise at least a functional portion of a polypeptide having an amino acid sequence selected from the group consisting of sequences provided in SEQ ID NO: 120-197, 275-348, 373-398, 406-409,

and variants thereof. As used herein, the "functional portion" of a polypeptide is that portion which contains the active site essential for affecting the function of the polypeptide, for example, the portion of the molecule that is capable of binding one or more reactants. The active site may be made up of separate portions present on one or more polypeptide chains and will generally exhibit high binding affinity.

Functional portions of a polypeptide may be identified by first preparing fragments of the polypeptide by either chemical or enzymatic digestion of the polypeptide, or by mutation analysis of the polynucleotide that encodes the polypeptide and subsequent expression of the resulting mutant polypeptides. The polypeptide fragments or mutant polypeptides are then tested to determine which portions retain biological activity, using, for example, the representative assays provided below.

Portions and other variants of the inventive polypeptides may also be generated by synthetic or recombinant means. Synthetic polypeptides having fewer than about 100 amino acids, and generally fewer than about 50 amino acids, may be generated using techniques well known to those of ordinary skill in the art. For example, such polypeptides may be synthesized using any of the commercially available solid-phase techniques, such as the Merrifield solid-phase synthesis method, where amino acids are sequentially added to a growing amino acid chain. *See* Merrifield, *J. Am. Chem. Soc.* 85:2149-2146, 1963. Equipment for automated synthesis of polypeptides is commercially available from suppliers such as Perkin Elmer/Applied BioSystems, Inc. (Foster City, California), and may be operated according to the manufacturer's instructions. Variants of a native polypeptide may be prepared using standard mutagenesis techniques, such as oligonucleotide-directed site-specific mutagenesis (Kunkel, T., *Proc. Natl. Acad. Sci. USA* 82:488-492, 1985). Sections of DNA sequence may also be removed using standard techniques to permit preparation of truncated polypeptides.

In general, the polypeptides disclosed herein are prepared in an isolated, substantially pure, form. Preferably, the polypeptides are at least about 80% pure, more preferably at least about 90% pure, and most preferably at least about 99% pure. In certain preferred embodiments, described in detail below, the isolated polypeptides are

incorporated into pharmaceutical compositions or vaccines for use in the treatment of skin disorders.

As used herein, the term "variant" comprehends nucleotide or amino acid sequences different from the specifically identified sequences, wherein one or more nucleotides or amino acid residues is deleted, substituted, or added. Variants may be naturally occurring allelic variants, or non-naturally occurring variants. Variant sequences (polynucleotide or polypeptide) preferably exhibit at least 50%, more preferably at least 75%, and most preferably at least 90% identity to a sequence of the present invention. The percentage identity is determined by aligning the two sequences to be compared as described below, determining the number of identical residues in the aligned portion, dividing that number by the total number of residues in the inventive (queried) sequence, and multiplying the result by 100.

Polynucleotide or polypeptide sequences may be aligned, and percentage of identical nucleotides in a specified region may be determined against another polynucleotide or polypeptide, using computer algorithms that are publicly available. Two exemplary algorithms for aligning and identifying the similarity of polynucleotide sequences are the BLASTN and FASTA algorithms. The alignment and similarity of polypeptide sequences may be examined using the BLASTP and algorithm. BLASTX and FASTX algorithms compare nucleotide query sequences translated in all reading frames against polypeptide sequences. The BLASTN, BLASTP and BLASTX algorithms are available on the NCBI anonymous FTP server (ftp://ncbi.nlm.nih.gov) under /blast/executables/. The FASTA and FASTX algorithms are available on the Internet at the ftp site ftp://ftp.virginia.edu/pub/. The FASTA algorithm, set to the default parameters described in the documentation and distributed with the algorithm, may be used in the determination of polynucleotide variants. The readme files for FASTA and FASTX v1.0x that are distributed with the algorithms describe the use of the algorithms and describe the default parameters. The use of the FASTA and FASTX algorithms is also described in Pearson, WR and Lipman, DJ, "Improved Tools for Biological Sequence Analysis," *PNAS* 85:2444-2448, 1988; and Pearson WR, "Rapid and Sensitive Sequence Comparison with FASTP and FASTA," *Methods in Enzymology* 183:63-98, 1990.

The BLASTN algorithm version 2.0.4 [Feb-24-1998], set to the default parameters described in the documentation and distributed with the algorithm, is preferred for use in the determination of polynucleotide variants according to the present invention. The BLASTP algorithm version 2.0.4, set to the default parameters described in the documentation and distributed with the algorithm, is preferred for use in the determination of polypeptide variants according to the present invention. The use of the BLAST family of algorithms, including BLASTN, BLASTP and BLASTX is described at NCBI's website at URL http://www.ncbi.nlm.nih.gov/BLAST/newblast.html and in the publication of Altschul, Stephen F., *et al.*, "Gapped BLAST and PSI-BLAST: a new generation of protein database search programs," *Nucleic Acids Res.* 25:3389-3402, 1997.

The following running parameters are preferred for determination of alignments and similarities using BLASTN that contribute to the E values and percentage identity for polynucleotides: Unix running command with default parameters thus: blastall -p blastn -d embldb -e 10 -G 0 -E 0 -r 1 -v 30 -b 30 -i queryseq –o results; and parameters are: -p Program Name [String]; -d Database [String]; -e Expectation value (E) [Real]; -G Cost to open a gap (zero invokes default behavior) [Integer]; -E Cost to extend a gap (zero invokes default behavior) [Integer]; -r Reward for a nucleotide match (blastn only) [Integer]; -v Number of one-line descriptions (V) [Integer]; -b Number of alignments to show (B) [Integer]; -i Query File [File In]; -o BLAST report Output File [File Out] Optional. The following running parameters are preferred for determination of alignments and similarities using BLASTP that contribute to the E values and percentage identity for polypeptides: blastall –p blastp –d swissprotdb –e 10 –G 1 –E 11 –r 1 –v 30 –b 30 –i queryseq –o results; and the parameters are: -p Program Name [String]; -d Database [String]; -e Expectation value (E) [Real]; -G Cost to open a gap (zero invokes default behavior) [Integer]; -E Cost to extend a gap (zero invokes default behavior) [Integer]; -v Number of one-line descriptions (v) [Integer]; -b Number of alignments to show (b) [Integer]; -I Query File [File In]; -o BLAST report Output File [File Out] Optional.

The "hits" to one or more database sequences by a queried sequence produced by BLASTN, BLASTP, FASTA, or a similar algorithm, align and identify similar portions of sequences. The hits are arranged in order of the degree of similarity and the length of

sequence overlap. Hits to a database sequence generally represent an overlap over only a fraction of the sequence length of the queried sequence.

The percentage similarity of a polynucleotide or polypeptide sequence is determined by aligning polynucleotide and polypeptide sequences using appropriate algorithms, such as BLASTN or BLASTP, respectively, set to default parameters; identifying the number of identical nucleic or amino acids over the aligned portions; dividing the number of identical nucleic or amino acids by the total number of nucleic or amino acids of the polynucleotide or polypeptide of the present invention; and then multiplying by 100 to determine the percentage similarity. By way of example, a queried polynucleotide having 220 nucleic acids has a hit to a polynucleotide sequence in the EMBL database having 520 nucleic acids over a stretch of 23 nucleotides in the alignment produced by the BLASTN algorithm using the default parameters. The 23 nucleotide hit includes 21 identical nucleotides, one gap and one different nucleotide. The percentage identity of the queried polynucleotide to the hit in the EMBL database is thus 21/220 times 100, or 9.5%. The similarity of polypeptide sequences may be determined in a similar fashion.

The BLASTN and BLASTX algorithms also produce "Expect" values for polynucleotide and polypeptide alignments. The Expect value (E) indicates the number of hits one can "expect" to see over a certain number of contiguous sequences by chance when searching a database of a certain size. The Expect value is used as a significance threshold for determining whether the hit to a database indicates true similarity. For example, an E value of 0.1 assigned to a polynucleotide hit is interpreted as meaning that in a database of the size of the EMBL database, one might expect to see 0.1 matches over the aligned portion of the sequence with a similar score simply by chance. By this criterion, the aligned and matched portions of the sequences then have a probability of 90% of being the same. For sequences having an E value of 0.01 or less over aligned and matched portions, the probability of finding a match by chance in the EMBL database is 1% or less using the BLASTN algorithm. E values for polypeptide sequences may be determined in a similar fashion using various polypeptide databases, such as the SwissProt database.

According to one embodiment, "variant" polynucleotides and polypeptides, with reference to each of the polynucleotides and polypeptides of the present invention, preferably comprise sequences having the same number or fewer nucleic or amino acids than each of the polynucleotides or polypeptides of the present invention and producing an E value of 0.01 or less when compared to the polynucleotide or polypeptide of the present invention. That is, a variant polynucleotide or polypeptide is any sequence that has at least a 99% probability of being the same as the polynucleotide or polypeptide of the present invention, measured as having an E value of 0.01 or less using the BLASTN or BLASTX algorithms set at the default parameters. According to a preferred embodiment, a variant polynucleotide is a sequence having the same number or fewer nucleic acids than a polynucleotide of the present invention that has at least a 99% probability of being the same as the polynucleotide of the present invention, measured as having an E value of 0.01 or less using the BLASTN algorithm set at the default parameters. Similarly, according to a preferred embodiment, a variant polypeptide is a sequence having the same number or fewer amino acids than a polypeptide of the present invention that has at least a 99% probability of being the same as the polypeptide of the present invention, measured as having an E value of 0.01 or less using the BLASTP algorithm set at the default parameters.

Variant polynucleotide sequences will generally hybridize to the recited polynucleotide sequences under stringent conditions. As used herein, "stringent conditions" refers to prewashing in a solution of 6X SSC, 0.2% SDS; hybridizing at 65°C, 6X SSC, 0.2% SDS overnight; followed by two washes of 30 minutes each in 1X SSC, 0.1% SDS at 65 °C and two washes of 30 minutes each in 0.2X SSC, 0.1% SDS at 65 °C.

As used herein, the term "*x*-mer," with reference to a specific value of "*x*," refers to a polynucleotide or polypeptide, respectively, comprising at least a specified number ("*x*") of contiguous residues of: any of the polynucleotides provided in SEQ ID NO: 1-119, 198-274, 349-372 and 399-405; or any of the polypeptides set out in SEQ ID NO: 120-197, 275-348, 373-398 and 406-409. The value of *x* may be from about 20 to about 600, depending upon the specific sequence.

Polynucleotides of the present invention comprehend polynucleotides comprising at least a specified number of contiguous residues (*x*-mers) of any of the polynucleotides identified as SEQ ID NO: 1-119, 198-274, 349-372 and 399-405, or their variants. Polypeptides of the present invention comprehend polypeptides comprising at least a specified number of contiguous residues (*x*-mers) of any of the polypeptides identified as SEQ ID NO: 120-197, 275-348, 373-398, and 406-409. According to preferred embodiments, the value of *x* is at least 20, more preferably at least 40, more preferably yet at least 60, and most preferably at least 80. Thus, polynucleotides of the present invention include polynucleotides comprising a 20-mer, a 40-mer, a 60-mer, an 80-mer, a 100-mer, a 120-mer, a 150-mer, a 180-mer, a 220-mer, a 250-mer; or a 300-mer, 400-mer, 500-mer or 600-mer of a polynucleotide provided in SEQ ID NO: 1-119, 198-274, 349-372 and 399-405 or a variant of one of the polynucleotides provided in SEQ ID NO: 1-119, 198-274, 349-372, and 399-405. Polypeptides of the present invention include polypeptides comprising a 20-mer, a 40-mer, a 60-mer, an 80-mer, a 100-mer, a 120-mer, a 150-mer, a 180-mer, a 220-mer, a 250-mer; or a 300-mer, 400-mer, 500-mer or 600-mer of a polypeptide provided in SEQ ID NO: 120-197, 275-348, 373-398, and 406-409, or a variant of one of the polynucleotides provided in SEQ ID NO: 120-197, 275-348, 373-398, and 406-409.

The inventive polynucleotides may be isolated by high throughput sequencing of cDNA libraries prepared from mammalian skin cells as described below in Example 1. Alternatively, oligonucleotide probes based on the sequences provided in SEQ ID NO: 1-119, 198-274, 349-372, and 399-405 can be synthesized and used to identify positive clones in either cDNA or genomic DNA libraries from mammalian skin cells by means of hybridization or polymerase chain reaction (PCR) techniques. Probes can be shorter than the sequences provided herein but should be at least about 10, preferably at least about 15 and most preferably at least about 20 nucleotides in length. Hybridization and PCR techniques suitable for use with such oligonucleotide probes are well known in the art (see, for example, Mullis, *et al.*, *Cold Spring Harbor Symp. Quant. Biol.*, 51:263, 1987; Erlich, ed., *PCR Technology*, Stockton Press: NY, 1989; (Sambrook, J, Fritsch, EF and Maniatis, T, eds., *Molecular Cloning: A Laboratory Manual*, 2nd ed., Cold Spring

Harbor Laboratory Press, Cold Spring Harbor: New York, 1989). Positive clones may be analyzed by restriction enzyme digestion, DNA sequencing or the like.

In addition, DNA sequences of the present invention may be generated by synthetic means using techniques well known in the art. Equipment for automated synthesis of oligonucleotides is commercially available from suppliers such as Perkin Elmer/Applied Biosystems Division (Foster City, California) and may be operated according to the manufacturer's instructions.

Since the polynucleotide sequences of the present invention have been derived from skin, they likely encode proteins that have important roles in growth and development of skin, and in responses of skin to tissue injury and inflammation as well as disease states. Some of the polynucleotides contain sequences that code for signal sequences, or transmembrane domains, which identify the protein products as secreted molecules or receptors. Such protein products are likely to be growth factors, cytokines, or their cognate receptors. Several of the polypeptide sequences have more than 25% similarity to known biologically important proteins and thus are likely to represent proteins having similar biological functions.

In particular, the inventive polypeptides have important roles in processes such as: induction of hair growth; differentiation of skin stem cells into specialized cell types; cell migration; cell proliferation and cell-cell interaction. The polypeptides are important in the maintenance of tissue integrity, and thus are important in processes such as wound healing. Some of the disclosed polypeptides act as modulators of immune responses, especially since immune cells are known to infiltrate skin during tissue insult causing growth and differentiation of skin cells. In addition, many polypeptides are immunologically active, making them important therapeutic targets in a whole range of disease states not only within skin, but also in other tissues of the body. Antibodies to the polypeptides of the present invention and small molecule inhibitors related to the polypeptides of the present invention may also be used for modulating immune responses and for treatment of diseases according to the present invention.

In one aspect, the present invention provides methods for using one or more of the inventive polypeptides or polynucleotides to treat disorders in a patient. As used herein, a "patient" refers to any warm-blooded animal, preferably a human.

In this aspect, the polypeptide or polynucleotide is generally present within a pharmaceutical composition or a vaccine. Pharmaceutical compositions may comprise one or more polypeptides, each of which may contain one or more of the above sequences (or variants thereof), and a physiologically acceptable carrier. Vaccines may comprise one or more of the above polypeptides and a non-specific immune response amplifier, such as an adjuvant or a liposome, into which the polypeptide is incorporated.

Alternatively, a vaccine or pharmaceutical composition of the present invention may contain DNA encoding one or more polypeptides as described above, such that the polypeptide is generated *in situ*. In such vaccines and pharmaceutical compositions, the DNA may be present within any of a variety of delivery systems known to those of ordinary skill in the art, including nucleic acid expression systems, and bacterial and viral expression systems. Appropriate nucleic acid expression systems contain the necessary DNA sequences for expression in the patient (such as a suitable promoter and terminator signal). Bacterial delivery systems involve the administration of a bacterium (such as Bacillus-Calmette-Guerin) that expresses an immunogenic portion of the polypeptide on its cell surface. In a preferred embodiment, the DNA may be introduced using a viral expression system (*e.g.*, vaccinia or other poxvirus, retrovirus, or adenovirus), which may involve the use of a non-pathogenic, or defective, replication competent virus. Techniques for incorporating DNA into such expression systems are well known in the art. The DNA may also be "naked," as described, for example, in Ulmer, *et al.*, *Science* 259:1745-1749, 1993 and reviewed by Cohen, *Science* 259:1691-1692, 1993. The uptake of naked DNA may be increased by coating the DNA onto biodegradable beads, which are efficiently transported into the cells.

Routes and frequency of administration, as well as dosage, will vary from individual to individual. In general, the pharmaceutical compositions and vaccines may be administered by injection (*e.g.*, intradermal, intramuscular, intravenous, or subcutaneous), intranasally (*e.g.*, by aspiration) or orally. In general, the amount of polypeptide present in a dose (or produced *in situ* by the DNA in a dose) ranges from about 1 pg to about 100 mg per kg of host, typically from about 10 pg to about 1 mg per kg of host, and preferably from about 100 pg to about 1 μg per kg of host. Suitable dose

sizes will vary with the size of the patient, but will typically range from about 0.1 ml to about 5 ml.

While any suitable carrier known to those of ordinary skill in the art may be employed in the pharmaceutical compositions of this invention, the type of carrier will vary depending on the mode of administration. For parenteral administration, such as subcutaneous injection, the carrier preferably comprises water, saline, alcohol, a lipid, a wax, or a buffer. For oral administration, any of the above carriers or a solid carrier, such as mannitol, lactose, starch, magnesium stearate, sodium saccharine, talcum, cellulose, glucose, sucrose, and magnesium carbonate, may be employed. Biodegradable microspheres (*e.g.*, polylactic galactide) may also be employed as carriers for the pharmaceutical compositions of this invention. Suitable biodegradable microspheres are disclosed, for example, in U.S. Patent Nos. 4,897,268 and 5,075,109.

Any of a variety of adjuvants may be employed in the vaccines derived from this invention to non-specifically enhance the immune response. Most adjuvants contain a substance designed to protect the antigen from rapid catabolism, such as aluminum hydroxide or mineral oil, and a non-specific stimulator of immune responses, such as lipid A, *Bordetella pertussis,* or *M. tuberculosis*. Suitable adjuvants are commercially available as, for example, Freund's Incomplete Adjuvant and Freund's Complete Adjuvant (Difco Laboratories, Detroit, Michigan), and Merck Adjuvant 65 (Merck and Company, Inc., Rahway, New Jersey). Other suitable adjuvants include alum, biodegradable microspheres, monophosphoryl lipid A, and Quil A.

The polynucleotides of the present invention may also be used as markers for tissue, as chromosome markers or tags, in the identification of genetic disorders, and for the design of oligonucleotides for examination of expression patterns using techniques well known in the art, such as the microarray technology available from Synteni (Palo Alto, California). Partial polynucleotide sequences disclosed herein may be employed to obtain full length genes by, for example, screening of DNA expression libraries using hybridization probes or PCR primers based on the inventive sequences.

The polypeptides provided by the present invention may additionally be used in assays to determine biological activity, to raise antibodies, to isolate corresponding ligands or receptors, in assays to quantitatively determine levels of protein or cognate

corresponding ligand or receptor, as anti-inflammatory agents, and in compositions for skin, connective tissue and/or nerve tissue growth or regeneration.

Example 1

ISOLATION OF cDNA SEQUENCES FROM SKIN CELL EXPRESSION LIBRARIES

The cDNA sequences of the present invention were obtained by high-throughput sequencing of cDNA expression libraries constructed from specialized rodent or human skin cells as shown in Table 1.

Table 1

Library	Skin cell type	Source
DEPA	dermal papilla	rat
SKTC	keratinocytes	human
HNFF	neonatal foreskin fibroblast	human
MEMS	embryonic skin	mouse
KSCL	keratinocyte stem cell	mouse
TRAM	transit amplifying cells	mouse

These cDNA libraries were prepared as described below.

cDNA Library from Dermal Papilla (DEPA)

Dermal papilla cells from rat hair vibrissae (whiskers) were grown in culture and the total RNA extracted from these cells using established protocols. Total RNA, isolated using TRIzol Reagent (BRL Life Technologies, Gaithersburg, Maryland), was used to obtain mRNA using a Poly(A) Quik mRNA isolation kit (Stratagene, La Jolla, California), according to the manufacturer's specifications. A cDNA expression library was then prepared from the mRNA by reverse transcriptase synthesis using a Lambda ZAP cDNA library synthesis kit (Stratagene).

cDNA Library from Keratinocytes (SKTC)

Keratinocytes obtained from human neonatal foreskins (Mitra, R and Nikoloff, B in *Handbook of Keratinocyte Methods*, pp. 17-24, 1994) were grown in serum-free KSFM (BRL Life Technologies) and harvested along with differentiated cells (10^8 cells). Keratinocytes were allowed to differentiate by addition of fetal calf serum at a final

concentration of 10% to the culture medium and cells were harvested after 48 hours. Total RNA was isolated from the two cell populations using TRIzol Reagent (BRL Life Technologies) and used to obtain mRNA using a Poly(A) Quik mRNA isolation kit (Stratagene). cDNAs expressed in differentiated keratinocytes were enriched by using a PCR-Select cDNA Subtraction Kit (Clontech, Palo Alto, California). Briefly, mRNA was obtained from either undifferentiated keratinocytes ("driver mRNA") or differentiated keratinocytes ("tester mRNA") and used to synthesize cDNA. The two populations of cDNA were separately digested with *Rsa*I to obtain shorter, blunt-ended molecules. Two tester populations were created by ligating different adaptors at the cDNA ends and two successive rounds of hybridization were performed with an excess of driver cDNA. The adaptors allowed for PCR amplification of only the differentially expressed sequences which were then ligated into T-tailed pBluescript (Hadjeb, N and Berkowitz, GA, *BioTechniques* 20:20-22 1996), allowing for a blue/white selection of cells containing vector with inserts. White cells were isolated and used to obtain plasmid DNA for sequencing.

cDNA library from human neonatal fibroblasts (HNFF)

Human neonatal fibroblast cells were grown in culture from explants of human neonatal foreskin and the total RNA extracted from these cells using established protocols. Total RNA, isolated using TRIzol Reagent (BRL Life Technologies, Gaithersburg, Maryland), was used to obtain mRNA using a Poly(A) Quik mRNA isolation kit (Stratagene, La Jolla, California), according to the manufacturer's specifications. A cDNA expression library was then prepared from the mRNA by reverse transcriptase synthesis using a Lambda ZAP cDNA library synthesis kit (Stratagene).

cDNA library from mouse embryonic skin (MEMS)

Embryonic skin was micro-dissected from day 13 post coitum Balb/c mice. Embryonic skin was washed in phosphate buffered saline and mRNA directly isolated from the tissue using the Quick Prep Micro mRNA purification kit (Pharmacia, Sweden). The mRNA was then used to prepare cDNA libraries as described above for the DEPA library.

cDNA library from mouse stem cells (KSCL) and transit amplifying (TRAM) cells

Pelts obtained from 1-2 day post-partum neonatal Balb/c mice were washed and

incubated in trypsin (BRL Life Technologies) to separate the epidermis from the dermis. Epidermal tissue was disrupted to disperse cells, which were then resuspended in growth medium and centrifuged over Percoll density gradients prepared according to the manufacturer's protocol (Pharmacia, Sweden). Pelleted cells were labeled using Rhodamine 123 (Bertoncello I, Hodgson GS and Bradley TR, *Exp Hematol.* 13:999-1006, 1985), and analyzed by flow cytometry (Epics Elite Coulter Cytometry, Hialeah, Florida). Single cell suspensions of rhodamine-labeled murine keratinocytes were then labeled with a cross reactive anti-rat CD29 biotin monoclonal antibody (Pharmingen, San Diego, California; clone Ha2/5). Cells were washed and incubated with anti-mouse CD45 phycoerythrin conjugated monoclonal antibody (Pharmingen; clone 30F11.1, 10ug/ml) followed by labeling with streptavidin spectral red (Southern Biotechnology, Birmingham, Alabama). Sort gates were defined using listmode data to identify four populations: CD29 bright rhodamine dull CD45 negative cells; CD29 bright rhodamine bright CD45 negative cells; CD29 dull rhodamine bright CD45 negative cells; and CD29 dull rhodamine dull CD45 negative cells. Cells were sorted, pelleted and snap frozen prior to storage at -80°C. This protocol was followed multiple times to obtain sufficient cell numbers of each population to prepare cDNA libraries. Skin stem cells and transit amplifying cells are known to express CD29, the integrin β1 chain. CD45, a leucocyte specific antigen, was used as a marker for cells to be excluded in the isolation of skin stem cells and transit amplifying cells. Keratinocyte stem cells expel the rhodamine dye more efficiently than transit amplifying cells. The CD29 bright, rhodamine dull, CD45 negative population (putative keratinocyte stem cells; referred to as KSCL), and the CD29 bright, rhodamine bright, CD45 negative population (keratinocyte transit amplifying cells; referred to as TRAM) were sorted and mRNA was directly isolated from each cell population using the Quick Prep Micro mRNA purification kit (Pharmacia, Sweden). The mRNA was then used to prepare cDNA libraries as described above for the DEPA library.

cDNA sequences were obtained by high-throughput sequencing of the cDNA libraries described above using a Perkin Elmer/Applied Biosystems Division Prism 377 sequencer.

Example 2

CHARACTERIZATION OF ISOLATED cDNA SEQUENCES

The isolated cDNA sequences were compared to sequences in the EMBL DNA database using the computer algorithms FASTA and/or BLASTN. The corresponding predicted protein sequences (DNA translated to protein in each of 6 reading frames) were compared to sequences in the SwissProt database using the computer algorithms FASTX and/or BLASTP. Comparisons of DNA sequences provided in SEQ ID NO: 1-119 to sequences in the EMBL DNA database (using FASTA) and amino acid sequences provided in SEQ ID NO: 120-197 to sequences in the SwissProt database (using FASTX) were made as of March 21, 1998. Comparisons of DNA sequences provided in SEQ ID NO: 198-274 to sequences in the EMBL DNA database (using BLASTN) and amino acid sequences provided in SEQ ID NO: 275-348 to sequences in the SwissProt database (using BLASTP) were made as of October 7, 1998. Comparisons of DNA sequences provided in SEQ ID NO: 349-372 to sequences in the EMBL DNA database (using BLASTN) and amino acid sequences provided in SEQ ID NO: 373-398 to sequences in the SwissProt database (using BLASTP) were made as of January 23, 1999.

Isolated cDNA sequences and their corresponding predicted protein sequences were computer analyzed for the presence of signal sequences identifying secreted molecules. Isolated cDNA sequences that have a signal sequence at a putative start site within the sequence are provided in SEQ ID NO: 1-44, 198-238, 349-358, and 399. The cDNA sequences of SEQ ID NO: 1-6, 198-199, 349-352, 354, and 356-358 were determined to have less than 75% identity (determined as described above), to sequences in the EMBL database using the computer algorithms FASTA or BLASTN, as described above. The predicted amino acid sequences of SEQ ID NO: 120-125, 275-276, 373-380, and 382 were determined to have less than 75% identity (determined as described above) to sequences in the SwissProt database using the computer algorithms FASTX or BLASTP, as described above.

Further sequencing of the some of the isolated partial cDNA sequences resulted in the isolation of the full-length cDNA sequences provided in SEQ ID NO: 7-14, 200-231, and 372. The corresponding predicted amino acid sequences are provided in SEQ ID NO: 126-133, 277-308, and 396, respectively. Comparison of the full length cDNA

sequences with those in the EMBL database using the computer algorithm FASTA or BLASTN, as described above, revealed less than 75% identity (determined as described above) to known sequences. Comparison of the predicted amino acid sequences provided in SEQ ID NO: 126-133 and 277-308 with those in the SwissProt database using the computer algorithms FASTX or BLASTP, as described above, revealed less than 75% identity (determined as described above) to known sequences.

Comparison of the predicted amino acid sequences corresponding to the cDNA sequences of SEQ ID NO: 15-23 with those in the EMBL using the computer algorithm FASTA database showed less than 75% identity (determined as described above) to known sequences. These predicted amino acid sequences are provided in SEQ ID NO: 134-142.

Further sequencing of some of the isolated partial cDNA sequences resulted in the isolation of full-length cDNA sequences provided in SEQ ID NO: 24-44 and 232-238. The corresponding predicted amino acid sequences are provided in SEQ ID NO: 143-163 and 309-315, respectively. These amino acid sequences were determined to have less than 75% identity, determined as described above to known sequences in the SwissProt database using the computer algorithm FASTX.

Isolated cDNA sequences having less than 75% identity to known expressed sequence tags (ESTs) or to other DNA sequences in the public database, or whose corresponding predicted protein sequence showed less than 75% identity to known protein sequences, were computer analyzed for the presence of transmembrane domains coding for putative membrane-bound molecules. Isolated cDNA sequences that have either one or more transmembrane domain(s) within the sequence are provided in SEQ ID NO: 45-63, 239-253, 359-364, 400-402. The cDNA sequences of SEQ ID NO: 45-48, 239-249, 359-361, and 363 were found to have less than 75% identity (determined as described above) to sequences in the EMBL database, using the FASTA or BLASTN computer algorithms. Their predicted amino acid sequences provided in SEQ ID NO: 164-167, 316-326, 383, 385-388 and 407-408 were found to have less than 75% identity, determined as described above, to sequences in the SwissProt database using the FASTX or BLASTP database.

Comparison of the predicted amino acid sequences corresponding to the cDNA sequences of SEQ ID NO: 49-63 and 250-253 with those in the SwissProt database showed less than 75% identity (determined as described above) to known sequences. These predicted amino acid sequences are provided in SEQ ID NO: 168-182 and 327-330.

Using automated search programs to screen against sequences coding for molecules reported to be of therapeutic and/or diagnostic use, some of the cDNA sequences isolated as described above in Example 1 were determined to encode predicted protein sequences that appear to be family members of known protein families. A family member is here defined to have at least 25% identity in the translated polypeptide to a known protein or member of a protein family. These cDNA sequences are provided in SEQ ID NO: 64-76, 254-264, 365-369, and 403, with the corresponding predicted amino acid sequences being provided in SEQ ID NO: 183-195, 331-341, 389-393 and 409, respectively. The cDNA sequences of SEQ ID NO: 64-68, 254-264, and 365-369 show less than 75% identity (determined as described above) to sequences in the EMBL database using the FASTA or BLASTN computer algorithms. Similarly, the amino acid sequences of SEQ ID NO: 183-195, 331-341, and 389-393 show less than 75% identity to sequences in the SwissProt database.

The likely utility for each of the proteins encoded by the DNA sequences of SEQ ID NO: 64-76, 254-264, 365-369, and 403, based on similarity to known proteins, is provided below:

Table 2

FUNCTIONS OF NOVEL PROTEINS

P/N SEQ ID NO:	A/A SEQ. ID NO.	SIMILARITY TO KNOWN PROTEINS
64 372	183 396	Slit, a secreted molecule required for central nervous system development
65	184	Immunoglobulin receptor family. About 40% of leucocyte membrane polypeptides contain immunoglobulin superfamily domains
66 403	185 409	RIP protein kinase, a serine/threonine kinase that contains a death domain to mediate apoptosis
67	186	Extracellular protein with epidermal growth factor domain capable of stimulating fibroblast proliferation
68	187	Transforming growth factor alpha, a protein which binds epidermal growth factor receptor and stimulates growth and mobility of keratinocytes
69	188	DRS protein which has a secretion signal component and whose expression is suppressed in cells transformed by oncogenes
70	189	A33 receptor with immunoglobulin-like domains and is expressed in greater than 95% of colon tumors
71	190	Interleukin-12 alpha subunit, component of a cytokine that is important in the immune defense against intracellular pathogens. IL-12 also stimulates proliferation and differentiation of TH1 subset of lymphocytes
72	191	Tumor Necrosis Factor receptor family of proteins that are involved in the proliferation, differentiation and death of many cell types including B and T lymphocytes.
73	192	Epidermal growth factor family proteins which stimulate growth and mobility of keratinocytes and epithelial cells. EGF is involved in wound healing. It also inhibits gastric acid secretion.
74	193	Fibronectin Type III receptor family. The fibronectin III domains are found on the extracellular regions of cytokine receptors
75	194	Serine/threonine kinases (STK2_HUMAN) which participate in cell cycle progression and signal transduction
76	195	Immunoglobulin receptor family
254	331	Receptor with immunoglobul in-like domains and homology to A33 receptor which is expressed in greater than 95% of colon tumors
255	332	Epidermal growth factor family proteins which stimulate growth and mobility of keratinocytes and epithelial cells. EGF is involved in wound healing. It also inhibits gastric acid secretion.

P/N SEQ ID NO:	A/A SEQ. ID NO.	SIMILARITY TO KNOWN PROTEINS
256	333	Serine/threonine kinases (STK2_HUMAN) which participate in cell cycle progression and signal transduction
257	334	Contains protein kinase and ankyrin domains. Possible role in cellular growth and differentiation.
258	335	Notch family proteins which are receptors involved in cellular differentiation.
259	336	Extracellular protein with epidermal growth factor domain capable of stimulating fibroblast proliferation.
260	337	Fibronectin Type III receptor family. The fibronectin III domains are found on the extracellular regions of cytokine receptors.
261	338	Immunoglobulin receptor family
262	339	ADP/ATP transporter family member containing a calcium binding site.
263	340	Mouse CXC chemokine family members are regulators of epithelial, lymphoid, myeloid, stromal and neuronal cell migration and cancers, agents for the healing of cancers, neuro-degenerative diseases, wound healing, inflammatory autoimmune diseases like psoriasis, asthma, Crohns disease and as agents for the prevention of HIV-1 of leukocytes
264	341	Nucleotide-sugar transporter family member.
365	389	Transforming growth factor betas (TGF-betas) are secreted covalently linked to latent TGF-beta-binding proteins (LTBPs). LTBPs are deposited in the extracellular matrix and play a role in cell growth or differentiation.
366	390	Integrins are Type I membrane proteins that function as laminin and collagen receptors and play a role in cell adhesion.
367	391	Integrins are Type I membrane proteins that function as laminin and collagen receptors and play a role in cell adhesion.
368	392	Cell wall protein precursor. Are involved in cellular growth or differentiation.
369	393	HT protein is a secreted glycoprotein with an EGF-like domain. It functions as a modulator of cell growth, death or differentiation.

These isolated sequences thus encode proteins that influence the growth, differentiation and activation of several cell types. They may usefully be developed as

agents for the treatment and diagnosis of skin wounds, cancers, growth and developmental defects, and inflammatory disease.

The polynucleotide sequences of SEQ ID NO: 77-117, 265-267, and 404-405 are differentially expressed in either keratinocyte stem cells (KSCL) or in transit amplified cells (TRAM) on the basis of the number of times these sequences exclusively appear in either one of the above two libraries; more than 9 times in one and none in the other (Audic S. and Claverie J-M, *Genome Research*, 7:986-995, 1997). The sequences of SEQ ID NO: 77-89, 265-267, and 365-369 were determined to have less than 75% identity to sequences in the EMBL and SwissProt databases using the computer algorithm FASTA or BLASTN, as described above. The proteins encoded by these polynucleotide sequences have utility as markers for identification and isolation of these cell types, and antibodies against these proteins may be usefully employed in the isolation and enrichment of these cells from complex mixtures of cells. Isolated polynucleotides and their corresponding proteins exclusive to the stem cell population can be used as drug targets to cause alterations in regulation of growth and differentiation of skin cells, or in gene targeting to transport specific therapeutic molecules to skin stem cells.

Example 3

ISOLATION AND CHARACTERIZATION OF THE HUMAN HOMOLOG OF MUTR1

The human homolog of muTR1 (SEQ ID NO: 68), obtained as described above in Example 1, was isolated by screening 50,000 pfu's of an oligo dT primed HeLa cell cDNA library. Plaque lifts, hybridization, and screening were performed using standard molecular biology techniques (Sambrook, J, Fritsch, EF and Maniatis, T, eds., *Molecular Cloning: A Laboratory Manual*, 2nd ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor: New York, 1989). The determined cDNA sequence of the isolated human homolog (huTR1) is provided in SEQ ID NO: 118, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 196. The library was screened using an [α ^{32}P]-dCTP labeled double stranded cDNA probe corresponding to nucleotides 1 to 459 of the coding region within SEQ ID NO: 118.

The polypeptide sequence of huTR1 has regions similar to Transforming Growth Factor-alpha, indicating that this protein functions like an epidermal growth factor (EGF).

This EGF-like protein will serve to stimulate keratinocyte growth and motility, and to inhibit the growth of epithelial-derived cancer cells. This novel gene and its encoded protein may thus be used as agents for the healing of wounds and regulators of epithelial-derived cancers.

Analysis of RNA transcripts by Northern Blotting

Northern analysis to determine the size and distribution of mRNA for huTR1 was performed by probing human tissue mRNA blots (Clontech) with a probe comprising nucleotides 93-673 of SEQ ID NO: 118, radioactively labeled with $[\alpha^{32}P]$-dCTP. Prehybridization, hybridization, washing and probe labeling were performed as described in Sambrook, *et al.*, *Ibid.* mRNA for huTR1 was 3.5-4kb in size and was observed to be most abundant in heart and placenta, with expression at lower levels being observed in spleen, thymus prostate and ovary (Fig. 1).

The high abundance of mRNA for huTR1 in the heart and placenta indicates a role for huTR1 in the formation or maintenance of blood vessels, as heart and placental tissues have an increased abundance of blood vessels, and therefore endothelial cells, compared to other tissues in the body. This, in turn, demonstrates a role for huTR1 in angiogenesis and vascularization of tumors. This is supported by the ability of Transforming Growth Factor-alpha and EGF to induce *de novo* development of blood vessels (Schreiber, *et al.*, *Science* 232:1250-1253, 1986) and stimulate DNA synthesis in endothelial cells (Schreiber, *et al.*, *Science* 232:1250-1253, 1986), and their over-expression in a variety of human tumors.

Purification of muTR1 and huTR1

Polynucleotides 177-329 of muTR1 (SEQ ID NO: 268), encoding amino acids 53-103 of muTR1 (SEQ ID NO: 342), and polynucleotides 208-360 of huTR1 (SEQ ID NO: 269), encoding amino acids 54-104 of huTR1 (SEQ ID NO: 343), were cloned into the bacterial expression vector pProEX HT (BRL Life Technologies), which contains a bacterial leader sequence and N-terminal 6xHistidine tag. These constructs were transformed into competent XL1-Blue *E. coli* as described in Sambrook et al., *Ibid.*

Starter cultures of these recombinant XL1-Blue *E. coli* were grown overnight at 37°C in Terrific broth containing 100 μg/ml ampicillin. This culture was spun down and

used to inoculate 500 ml culture of Terrific broth containing 100 μg/ml ampicillin. Cultures were grown until the OD_{595} of the cells was between 0.4 and 0.8, whereupon IPTG was added to 1 mM. Cells were induced overnight and bacteria were harvested by centrifugation.

Both the polypeptide of muTR1 (SEQ ID NO: 342; referred to as muTR1a) and that of huTR1 (SEQ ID NO: 343; referred to as huTR1a) were expressed in insoluble inclusion bodies. In order to purify the polypeptides muTR1a and huTR1a, bacterial cell pellets were re-suspended in lysis buffer (20 mM Tris-HCl pH 8.0, 10 mM beta mercaptoethanol, 1 mM PMSF). To the lysed cells, 1% NP40 was added and the mix incubated on ice for 10 minutes. Lysates were further disrupted by sonication on ice at 95W for 4 x 15 seconds and then centrifuged for 15 minutes at 14,000 rpm to pellet the inclusion bodies.

The resulting pellet was re-suspended in lysis buffer containing 0.5% w/v CHAPS and sonicated on ice for 5-10 seconds. This mix was stored on ice for 1 hour, centrifuged at 14,000 rpm for 15 minutes at 4 °C and the supernatant discarded. The pellet was once more re-suspended in lysis buffer containing 0.5% w/v CHAPS, sonicated, centrifuged and the supernatant removed as before. The pellet was re-suspended in solubilizing buffer (6 M Guanidine HCl, 0.5 M NaCl, 20 mM Tris HCl, pH 8.0), sonicated at 95 W for 4 x 15 seconds and then centrifuged for 20 minutes at 14,000 rpm and 4 °C to remove debris. The supernatant was stored at 4 °C until use.

Polypeptides muTR1a and huTR1a were purified by virtue of the N-terminal 6x Histidine tag contained within the bacterial leader sequence, using a Nickel-Chelating Sepharose column (Amersham Pharmacia, Uppsala, Sweden) and following the manufacturer's recommended protocol. In order to refold the proteins once purified, the protein solution was added to 5x its volume of refolding buffer (1 mM EDTA, 1.25 mM reduced glutathione, 0.25 mM oxidised glutathione, 20 mM Tris-HCl, pH 8.0) over a period of 1 hour at 4 °C. The refolding buffer was stirred rapidly during this time, and stirring continued at 4 °C overnight. The refolded proteins were then concentrated by ultrafiltration using standard protocols.

Biological Activities of Polypeptides muTR1a and huTR1a

muTR1 and huTR1 are novel members of the EGF family, which includes EGF, TGFα, epiregulin and others. These growth factors are known to act as ligands for the EGF receptor. The pathway of EGF receptor activation is well documented. Upon binding of a ligand to the EGF receptor, a cascade of events follows, including the phosphorylation of proteins known as MAP kinases. The phosphorylation of MAP kinase can thus be used as a marker of EGF receptor activation. Monoclonal antibodies exist which recognize the phosphorylated forms of 2 MAP kinase proteins – ERK1 and ERK2.

In order to examine whether purified polypeptides of muTR1a and huTR1a act as a ligand for the EGF receptor, cells from the human epidermal carcinoma cell line A431 (American Type Culture Collection, No. CRL-1555, Manassas, Virginia) were seeded into 6 well plates, serum starved for 24 hours, and then stimulated with purified muTR1a or huTR1a for 5 minutes in serum free conditions. As a positive control, cells were stimulated in the same way with 10 to 100 ng/ml TGF-alpha or EGF. As a negative control, cells were stimulated with PBS containing varying amounts of LPS. Cells were immediately lysed and protein concentration of the lysates estimated by Bradford assay. 15 μg of protein from each sample was loaded onto 12% SDS-PAGE gels. The proteins were then transferred to PVDF membrane using standard techniques.

For Western blotting, membranes were incubated in blocking buffer (10mM Tris-HCl, pH 7.6, 100 mM NaCl, 0.1% Tween-20, 5% non-fat milk) for 1 hour at room temperature. Rabbit anti-Active MAP kinase pAb (Promega, Madison, Wisconsin) was added to 50 ng/ml in blocking buffer and incubated overnight at 4 °C. Membranes were washed for 30 mins in blocking buffer minus non-fat milk before being incubated with anti rabbit IgG-HRP antibody, at a 1:3500 dilution in blocking buffer, for 1 hour at room temperature. Membranes were washed for 30 minutes in blocking buffer minus non-fat milk, then once for 5 minutes in blocking buffer minus non-fat milk and 0.1% Tween-20. Membranes were then exposed to ECL reagents for 2 min, and then autoradiographed for 5 to 30 min.

As shown in Fig. 2, both muTR1a and huTR1a were found to induce the phosphorylation of ERK1 and ERK2 over background levels, indicating that muTR1 and

huTR1 act as ligands for a cell surface receptor that activates the MAP kinase signaling pathway, possibly the EGF receptor. As shown in Fig. 11, huTR1a was also demonstrated to induce the phosphorylation of ERK1 and ERK2 in CV1/EBNA kidney epithelial cells in culture, as compared with the negative control. These assays were conducted as described above. This indicates that huTR1a acts as a ligand for a cell surface receptor that activates the MAP kinase signaling pathway, possibly the EGF receptor in HeLa and CV1/EBNA cells.

The ability of muTR1a to stimulate the growth of neonatal foreskin (NF) keratinocytes was determined as follows. NF keratinocytes derived from surgical discards were cultured in KSFM (BRL Life Technologies) supplemented with bovine pituatary extract (BPE) and epidermal growth factor (EGF). The assay was performed in 96 well flat-bottomed plates in 0.1 ml unsupplemented KSFM. MuTR1a, human transforming growth factor alpha (huTGFα) or PBS-BSA was titrated into the plates and 1 x 10^3 NF keratinocytes were added to each well. The plates were incubated for 5 days in an atmosphere of 5% CO_2 at 37^0C. The degree of cell growth was determined by MTT dye reduction as described previously (*J. Imm. Meth.* 93:157-165, 1986). As shown in Fig. 3, both muTR1a and the positive control human TGFα stimulated the growth of NF keratinocytes, whereas the negative control, PBS-BSA, did not.

The ability of muTR1a and huTR1a to stimulate the growth of a transformed human keratinocyte cell line, HaCaT, was determined as follows. The assay was performed in 96 well flat-bottomed plates in 0.1 ml DMEM (BRL Life Technologies) supplemented with 0.2% FCS. MuTR1a, huTR1a and PBS-BSA were titrated into the plates and 1 x10^3 HaCaT cells were added to each well. The plates were incubated for 5 days in an atmosphere containing 10% CO_2 at 37^0C. The degree of cell growth was determined by MTT dye reduction as described previously (*J. Imm. Meth.* 93:157-165, 1986). As shown in Fig. 4, both muTR1a and huTR1a stimulated the growth of HaCaT cells, whereas the negative control PBS-BSA did not.

The ability of muTR1a and huTR1a to inhibit the growth of A431 cells was determined as follows. Polypeptides muTR1a (SEQ ID NO: 342) and huTR1a (SEQ ID NO: 343) and PBS-BSA were titrated as described previously (*J. Cell. Biol.* 93:1-4, 1982) and cell death determined using the MTT dye reduction as described previously

(*J. Imm. Meth.* 93:157-165, 1986). Both muTR1a and huTR1a were found to inhibit the growth of A431 cells, whereas the negative control PBS-BSA did not (Fig. 5).

These results indicate that muTR1 and huTR1 stimulate keratinocyte growth and motility, inhibit the growth of epithelial-derived cancer cells, and play a role in angiogenesis and vascularization of tumors. This novel gene and its encoded protein may thus be developed as agents for the healing of wounds, angiogenesis and regulators of epithelial-derived cancers.

Upregulation of huTR1 and mRNA expression

HeLa cells (human cervical adenocarcinoma) were seeded in 10 cm dishes at a concentration of 1 x 10^6 cells per dish. After incubation overnight, media was removed and replaced with media containing 100 ng/ml of muTR1, huTR1, huTGFα, or PBS as a negative control. After 18 hours, media was removed and the cells lysed in 2 ml of TRIzol reagent (Gibco BRL Life Technologies, Gaithersburg, Maryland). Total RNA was isolated according to the manufacturer's instructions. To identify mRNA levels of huTR1 from the cDNA samples, 1 μl of cDNA was used in a standard PCR reaction. After cycling for 30 cycles, 5 μl of each PCR reaction was removed and separated on a 1.5% agarose gel. Bands were visualized by ethidium bromide staining. As can be seen from Fig. 12, both mouse and human TR1 up-regulate the mRNA levels of huTR1 as compared with cells stimulated with the negative control of PBS. Furthermore, TGFα can also up-regulate the mRNA levels of huTR1.

These results indicate that TR1 is able to sustain its own mRNA expression and subsequent protein expression, and thus is expected to be able to contribute to the progression of diseases such as psoriasis where high levels of cytokine expression are involved in the pathology of the disease. Furthermore, since TGFα can up-regulate the expression of huTR1, the up-regulation of TR1 mRNA may be critical to the mode of action of TGFα.

Serum response element reporter gene assay

The serum response element (SRE) is a promoter element required for the regulation of many cellular immediate-early genes by growth. Studies have demonstrated that the activity of the SRE can be regulated by the MAP kinase signaling pathway. Two cell lines, PC12 (rat pheochromocytoma – neural tumor) and HaCaT (human transformed

keratinocytes), containing eight SRE upstream of an SV40 promotor and luciferase reporter gene were developed in-house. 5 x 10^3 cells were aliquoted per well of 96 well plate and grown for 24 hours in their respective media. HaCaT SRE cells were grown in 5% fetal bovine serum (FBS) in D-MEM supplemented with 2mM L-glutamine (Sigma, St. Louis, Missouri), 1mM sodium pyruvate (BRL Life Technologies), 0.77mM L-asparagine (Sigma), 0.2mM arginine (Sigma), 160mM penicillin G (Sigma), 70mM dihydrostreptomycin (Roche Molecular Biochemicals, Basel, Switzerland), and 0.5 mg/ml geneticin (BRL Life Technologies). PC12 SRE cells were grown in 5% fetal bovine serum in Ham F12 media supplemented with 0.4 mg/ml geneticin (BRL Life Technologies). Media was then changed to 0.1% FBS and incubated for a further 24 hours. Cells were then stimulated with a titration of TR1 from 1 μg/ml. A single dose of basic fibroblast growth factor at 100 ng/ml (R&D Systems, Minneapolis, Minnesota) or epidermal growth factor at 10 ng/ml (BRL Life Technologies) was used as a positive control. Cells were incubated in the presence of muTR1 or positive control for 6 hours, washed twice in PBS and lysed with 40 μl of lysis buffer (Promega). 10 μl was transferred to a 96 well plate and 10 μl of luciferase substrate (Promega) added by direct injection into each well by a Victor^2 fluorimeter (Wallac), the plate was shaken and the luminescence for each well read at 3x1 sec Intervals. Fold induction of SRE was calculated using the following equation: Fold induction of SRE = Mean relative luminescence of agonist/Mean relative luminescence of negative control.

As shown in Fig. 13, muTR1 activates the SRE in both PC-12 (Fig. 13a) and HaCaT (Fig. 13b) cells. This indicates that HaCaT and PC-12 cells are able to respond to muTR1 protein and elicit a response. In the case of HaCaT cells, this is a growth response. In the case of PC-12 cells, this may be a growth, a growth inhibition, differentiation, or migration response. Thus, TR1 may be important in the development of neural cells or their differentiation into specific neural subsets. TR1 may also be important in the development and progression of neural tumors.

Inhibition by the EGF receptor assay

The HaCaT growth assay was conducted as previously described, except that modifications were made as follows. Concurrently with the addition of EGF and TR1 to the media, anti-EGF Receptor (EGFR) antibody (Promega, Madison, Wisconsin) or

negative control antibody, mouse IgG (PharMingen, San Diego, California), were added at a concentration of 62.5 ng/ml.

As seen in Fig. 14, an antibody which blocks the function of the EGFR inhibits the mitogenicity of TR1 on HaCaT cells. This indicates that the EGFR is crucial for transmission of the TR1 mitogenic signal on HaCaT cells. TR1 may bind directly to the EGF receptor. TR1 may also bind to any other members of the EGFR family – ErbB-2, -3, and/or -4 – that are capable of heterodimerizing with the EGFR.

Sequence of splice variant of huTR1, huTR1β

A variant of huTR1 was isolated from the same library as huTR1 (SEQ ID NO: 118), following the same protocols. This sequence is a splice variant of huTR1 and consists of the ORF of huTR1 minus amino acids 87 to 137. This has the effect of deleting the third cysteine residue of the EGF motif and the transmembrane domain. However, cysteine residue 147 (huTR1 ORF numbering) may replace the deleted cysteine and thus the disulphide bridges are likely not affected. Therefore, huTR1β is a secreted form of huTR1. It functions as an agonist or an antagonist to huTR1 or other EGF family members, including EGF and TGFα. The determined nucleotide sequence of the splice variant of TR1, referred to as huTR1β, is given in SEQ ID NO: 371 and the corresponding predicted amino acid sequence is SEQ ID NO: 395.

Example 4

IDENTIFICATION, ISOLATION AND CHARACTERIZATION OF DP3

A partial cDNA fragment, referred to as DP3, was identified by differential display RT-PCR (modified from Liang P and Pardee AB, *Science* 257:967-971, 1992) using mRNA from cultured rat dermal papilla and footpad fibroblast cells, isolated by standard cell biology techniques. This double stranded cDNA was labeled with [α^{32}P]-dCTP and used to identify a full length DP3 clone by screening 400,000 pfu's of an oligo dT-primed rat dermal papilla cDNA library. The determined full-length cDNA sequence for DP3 is provided in SEQ ID NO: 119, with the corresponding amino acid sequence being provided in SEQ ID NO: 197. Plaque lifts, hybridization and screening were performed using standard molecular biology techniques.

Example 5

ISOLATION AND CHARACTERIZATION OF THE HUMAN HOMOLOG OF MUKS1

Analysis of RNA transcripts by Northern Blotting

Northern analysis to determine the size and distribution of mRNA for muKS1 (SEQ ID NO: 263) was performed by probing murine tissue mRNA blots with a probe consisting of nucleotides 268-499 of muKS1, radioactively labeled with [α^{32}P]-dCTP. Prehybridization, hybridization, washing, and probe labeling were performed as described in Sambrook, *et al.*, *Ibid.* mRNA for muKS1 was 1.6 kb in size and was observed to be most abundant in brain, lung, muscle, and heart. Expression could also be detected in lower intestine, skin, and kidney. No detectable signal was found in testis, spleen, liver, thymus, stomach.

Human homologue of muKS1

MuKS1 (SEQ ID NO: 263) was used to search the EMBL database (Release 50, plus updates to June, 1998) to identify human EST homologues. The top three homologies were to the following ESTs: accession numbers AA643952, HS1301003 and AA865643. These showed 92.63% identity over 285 nucleotides, 93.64% over 283 nucleotides and 94.035% over 285 nucleotides, respectively. Frame shifts were identified in AA643952 and HS1301003 when translated. Combination of all three ESTs identified huKS1 (SEQ ID NO: 270) and translated polypeptide SEQ ID NO: 344. Alignment of muKS1 and huKS1 polypeptides indicated 95% identity over 96 amino acids.

Bacterial expression and purification of muKS1 and huKS1

Polynucleotides 269-502 of muKS1 (SEQ ID NO: 271), encoding amino acids 23-99 of polypeptide muKS1 (SEQ ID NO: 345), and polynucleotides 55-288 of huKS1 (SEQ ID NO: 272), encoding amino acids 19-95 of polypeptide huKS1 (SEQ ID NO: 346), were cloned into the bacterial expression vector pET-16b (Novagen, Madison, Wisconsin), which contains a bacterial leader sequence and N-terminal 6xHistidine tag. These constructs were transformed into competent XL1-Blue *E. coli* as described in Sambrook et al., *Ibid.*

Starter cultures of recombinant BL 21 (DE3) *E. coli* (Novagen) containing SEQ ID NO: 271 (muKS1a) and SEQ ID NO: 272 (huKS1a) were grown in NZY broth containing 100 μg/ml ampicillin (Gibco-BRL Life Technologies) at 37°C. Cultures were spun down and used to inoculate 800 ml of NZY broth and 100 μg/ml ampicillin. Cultures were grown until the OD_{595} of the cells was between 0.4 and 0.8. Bacterial expression was induced for 3 hours with 1 mM IPTG. Bacterial expression produced an induced band of approximately 15kDa for muKS1a and huKS1a.

MuKS1a and huKS1a were expressed in insoluble inclusion bodies. In order to purify the polypeptides, bacterial cell pellets were re-suspended in lysis buffer (20 mM Tris-HCl pH 8.0, 10 mM βMercaptoethanol, 1 mM PMSF). To the lysed cells, 1% NP-40 was added and the mix incubated on ice for 10 minutes. Lysates were further disrupted by sonication on ice at 95 W for 4 x 15 seconds and then centrifuged for 10 minutes at 18,000 rpm to pellet the inclusion bodies.

The pellet containing the inclusion bodies was re-suspended in lysis buffer containing 0.5% w/v CHAPS and sonicated for 5-10 seconds. This mix was stored on ice for 1 hour, centrifuged at 14000 rpm for 15 minutes at 4°C and the supernatant discarded. The pellet was once more re-suspended in lysis buffer containing 0.5% w/v CHAPS, sonicated, centrifuged, and the supernatant removed as before. The pellet was re-suspended in solubilizing buffer (6 M guanidine HCl, 0.5 M NaCl, 20 mM Tris-HCl pH 8.0), sonicated at 95W for 4 x 15 seconds and centrifuged for 10 minutes at 18000 rpm and 4°C to remove debris. The supernatant was stored at 4°C. MuKS1a and huKS1a were purified by virtue of the N-terminal 6x histidine tag contained within the bacterial leader sequence, using a Nickel-Chelating sepharose column (Amersham Pharmacia, Uppsala, Sweden) and following the manufacturer's protocol. Proteins were purified twice over the column to reduce endotoxin contamination. In order to re-fold the proteins once purified, the protein solution was dialysed in a 4 M-2 M urea gradient in 20 mM tris-HCl pH 7.5 + 10% glycerol overnight at 4°C. The protein was then further dialysed 2x against 2 litres of 20 mM Tris-HCl pH 7.5 + 10% glycerol.

Peptide sequencing of muKS1 and huKS1

Bacterially expressed muKS1 and huKS1 were separated on polyacrylamide gels and induced bands of 15 kDa were identified. The predicted size of muKS1 is 9.4 kDa.

To obtain the amino acid sequence of the 15 kDa bands, 20 μg recombinant muKS1 and huSK1 was resolved by SDS-PAGE and electroblotted onto Immobilon PVDF membrane (Millipore, Bedford, Massachusetts). Internal amino acid sequencing was performed on tryptic peptides of muKS1 and huKS1 by the Protein Sequencing Unit at the University of Auckland, New Zealand.

The determined amino acid sequences for muKS1 and huKS1 are given in SEQ ID NOS: 397 and 398, respectively. These amino acid sequences confirmed that the determined sequences are identical to that predicted from the cDNA sequences. The size discrepancy has previously been reported for other chemokines (Richmond A, Balentien E, Thomas HG, Flaggs G, Barton DE, Spiess J, Bordoni R, Francke U, Derynck R, "Molecular characterization and chromosomal mapping of melanoma growth stimulatory activity, a growth factor structurally related to beta-thromboglobulin," *EMBO J.* 7:2025-2033, 1988; Liao F, Rabin RL, Yannelli JR, Koniaris LG, Vanguri P, Farber JM, "Human Nig chemokine: biochemical and functional characterization," *J. Exp. Med.* 182:1301-1314, 1995). The isoelectric focusing point of these proteins was predicted to be 10.26 using DNASIS (HITACHI Software Engineering, San Francisco, California).

Oxidative burst assay

Oxidative burst assays were used to determine responding cell types. 1 x 10^7 PBMC cells were resuspended in 5 ml HBSS, 20mM HEPES, 0.5% BSA and incubated for 30 minutes at 37°C with 5 μl 5 mM dichloro-dihydrofluorescein diacetate (H_2DCFDA, Molecular Probes, Eugene, Oregon). 2 x 10^5 H_2DCFDA-labeled cells were loaded in each well of a flat-bottomed 96 well plate. 10 μl of each agonist was added simultaneously into the well of the flat-bottomed plate to give final concentrations of 100 ng/ml (fMLP was used at 10 μM). The plate was then read on a Victor^2 1420 multilabel counter (Wallac, Turku, Finland) with a 485 nm excitation wavelength and 535 nm emission wavelength. Relative fluorescence was measured at 5 minute intervals over 60 minutes.

A pronounced respiratory burst was identified in PBMC with a 2.5 fold difference between control treated cells (TR1) and cells treated with 100 ng/ml muKS1 (Fig. 8).

Human stromal derived factor-1α (SDF1α) (100 ng/ml) and 10 μM formyl-Met-Leu-Phe (fMLP) were used as positive controls.

Chemotaxis assay

Cell migration in response to muKS1 was tested using a 48 well Boyden's chamber (Neuro Probe Inc., Cabin John, Maryland) as described in the manufacturer's protocol. In brief, agonists were diluted in HBSS, 20mM HEPES, 0.5% BSA and added to the bottom wells of the chemotactic chamber. THP-1 cells were re-suspended in the same buffer at 3×10^5 cells per 50 μl. Top and bottom wells were separated by a PVP-free polycarbonate filter with a 5 μm pore size for monocytes or 3 μm pore size for lymphocytes. Cells were added to the top well and the chamber incubated for 2 hours for monocytes and 4 hours for lymphocytes in a 5% CO_2 humidified incubator at 37°C. After incubation, the filter was fixed and cells scraped from the upper surface. The filter was then stained with Diff-Quick (Dade International Inc., Miami, Florida) and the number of migrating cells counted in five randomly selected high power fields. The results are expressed as a migration index (the number of test migrated cells divided by the number of control migrated cells).

Using this assay, muKS1 was tested against T cells and THP-1 cells. MuKS1 induced a titrateable chemotactic effect on THP-1 cells from 0.01 ng/ml to 100 ng/ml (Fig. 9). Human SDF1α was used as a positive control and gave an equivalent migration. MuKS1 was also tested against IL-2 activated T cells. However, no migration was evidence for muKS1 even at high concentrations, whereas SDF-1α provided an obvious titrateable chemotactic stimulus. Therefore, muKS1 appears to be chemotactic for THP-1 cells but not for IL-2 activated T cells at the concentrations tested.

Full length sequence of muKS1 clone

The nucleotide sequence of muKS1 was extended by determining the base sequence of additional ESTs. Combination of all the ESTs identified the full-length muKS1 (SEQ ID NO: 370) and the corresponding translated polypeptide sequence in SEQ ID NO: 394.

Analysis of human RNA transcripts by Northern blotting

Northern blot analysis to determine the size and distribution of mRNA for the human homologue of muKS1 was performed by probing human tissue blots (Clontech,

Palo Alto, California) with a radioactively labeled probe consisting of nucleotides 1 to 288 of huKS1 (SEQ ID NO: 270). Prehybridization, hybridization, washing, and probe labeling were performed as described in Sambrook, *et al., Ibid.* mRNA for huKS1 was 1.6 kb in size and was observed to be most abundance in kidney, liver, colon, small intestine, and spleen. Expression could also be detected in pancreas, skeletal muscle, placenta, brain, heart, prostate, and thymus. No detectable signal was found in lung, ovary, and testis.

Analysis of human RNA transcripts in tumor tissue by Northern blotting

Northern blot analysis to determine distribution of huKS1 in cancer tissue was performed as described previously by probing tumor panel blots (Invitrogen, Carlsbad, California). These blots make a direct comparison between normal and tumor tissue. MRNA was observed in normal uterine and cervical tissue but not in the respective tumor tissue. In contrast, expression was up-regulated in breast tumor and down-regulated in normal breast tissue. No detectable signal was found in either ovary or ovarian tumors.

Injection of bacterially expressed muKS1a into nude mice

Two nude mice were anaesthetised intraperitoneally with 75 µl of 1/10 dilution of Hypnorm (Janssen Pharmaceuticals, Buckinghamshire, England) in phosphate buffered saline. 20ug of bacterially expressed muKS1a (SEQ ID NO: 345) was injected subcutaneously in the left hind foot, ear and left-hand side of the back. The same volume of phosphate buffered saline was injected in the same sites but on the right-hand side of the same animal. Mice were left for 18 hours and then examined for inflammation. Both mice showed a red swelling in the ear and foot sites injected with the bacterially expressed protein. No obvious inflammation could be identified in either back site. Mice were culled and biopsies taken from the ear, back and foot sites and fixed in 3.7% formol saline. Biopsies were embedded, sectioned and stained with Haemotoxylin and eosin. Sites injected with muKS1a had a marked increase in polymorphonuclear granulocytes, whereas sites injected with phosphate buffered saline had a low background infiltrate of polymorphonuclear granulocytes.

Injection of bacterially recombinant muKS1 into C3H/HeJ mice

Eighteen C3H/HeJ mice were divided into 3 groups and injected intraperitoneally with muKS1, GV14B, or phosphate buffered saline (PBS). GV14B is a bacterially

expressed recombinant protein used as a negative control. Group 1 mice were injected with 50 μg of muKS1 in 1 ml of PBS; Group 2 mice were injected with 50 μg of GV14B in 1 ml of PBS; and Group 3 mice with 1 ml of PBS. After 18 hours, the cells in the peritoneal cavity of the mice were isolated by intraperitoneal lavage with 2 x 4 ml washes with harvest solution (0.02% EDTA in PBS). Viable cells were counted from individual mice from each group. Mice injected with 50 μg of muKS1 had on average a 3-fold increase in cell numbers (Fig. 10).

20 μg of bacterial recombinant muKS1 was injected subcutaneously into the left hind foot of three C3H/HeJ mice. The same volume of PBS was injected into the same site on the right-hand side of the same animal. After 18 hours, mice were examined for inflammation. All mice showed a red swelling in the foot pad injected with bacterially recombinant KS1. From histology, sites injected with muKS1 had an inflammatory response of a mixed phenotype with mononuclear and polymorphonuclear cells present.

Chemokines are a large superfamily of highly basic secreted proteins with a broad number of functions (Baggiolini, *et al.*, *Annu. Rev. Immunol.*, 15:675-705, 1997; Ward, *et al.*, *Immunity,* 9:1-11, 1998; Horuk, *Nature,* 393:524-525, 1998). The polypeptide sequences of muKS1 and huKS1 have similarity to CXC chemokines, suggesting that this protein will act like other CXC chemokines. The *in vivo* data from nude mice supports this hypothesis. This chemokine-like protein may therefore be expected to stimulate leukocyte, epithelial, stromal, and neuronal cell migration; promote angiogenesis and vascular development; promote neuronal patterning, hemopoietic stem cell mobilization, keratinocyte and epithelial stem cell patterning and development, activation and proliferation of leukocytes; and promotion of migration in wound healing events. It has recently been shown that receptors to chemokines act as co-receptors for HIV-1 infection of CD4+ cells (Cairns, *et al.*, *Nature Medicine,* 4:563-568, 1998) and that high circulating levels of chemokines can render a degree of immunity to those exposed to the HIV virus (Zagury, *et al.*, *Proc. Natl. Acad. Sci. USA* 95:3857-3861, 1998). This novel gene and its encoded protein may thus be usefully employed as regulators of epithelial, lymphoid, myeloid, stromal, and neuronal cells migration and cancers; as agents for the treatment of cancers, neuro-degenerative diseases, inflammatory autoimmune diseases

such as psoriasis, asthma and Crohn's disease for use in wound healing; and as agents for the prevention of HIV-1 binding and infection of leukocytes.

We have also shown that muKS1 can promote a quantifiable increase in cell numbers in the peritoneal cavity of C3H/HeJ mice injected with muKS1. Furthermore, we have shown that muKS1 can induce an oxidative burst in human peripheral blood mononuclear cells and migration in the human monocyte leukemia cell line, THP-1, suggesting that monocyte/macrophages are one of the responsive cell types for KS1. In addition to this, we demonstrated that huKS1 was expressed at high levels in a number of non-lymphoid tissues, such as the colon and small intestine, and in breast tumors. It was also expressed in normal uterine and cervical tissue, but was completely down-regulated in their respective tumors. It has recently been shown that non-ELR chemokines have demonstrated angiostatic properties. IP-10 and Mig, two non-ELR chemokines, have previously been shown to be up-regulated during regression of tumors (Tannenbaum CS, Tubbs R, Armstrong D, Finke JH, Bukowski RM, Hamilton TA, "The CXC Chemokines IP-10 and Mig are necessary for IL-12-mediated regression of the mouse RENCA tumor," *J. Immunol.* 161: 927-932, 1998), with levels of expression inversely correlating with tumor size (Kanegane C, Sgadari C, Kanegane H, Teruya-Feldstine J, Yao O, Gupta G, Farber JM, Liao F, Liu L, Tosato G, "Contribution of the CXC Chemokines IP-10 and Mig to the antitumor effects of IL-12," *J. Leuko. Biol.* 64: 384-392, 1998). Furthermore, neutralizing antibodies to IP-10 and Mig would reduce the anti-tumor effect, indicating the contribution these molecules make to the anti-tumor effects. Therefore, it is expected that in the case of cervical and uterine tumors, KS1 would have similar properties.

The data demonstrates that KS1 is involved in cell migration showing that one of the responsive cell types is monocyte/macrophage. The human expression data in conjunction with the *in vitro* and *in vivo* biology demonstrates that this molecule may be a useful regulator in cell migration, and as an agent for the treatment of inflammatory diseases, such as Crohn's disease, ulcerative colitis, and rheumatoid arthritis; and cancers, such as cervical adenocarcinoma, uterine leiomyoma, and breast invasive ductal carcinoma.

Example 6

CHARACTERIZATION OF KS2

KS2 contains a transmembrane domain and may function as either a membrane-bound ligand or a receptor. Northern analysis indicated that the mRNA for KS2 was expressed in the mouse keratinocyte cell line, Pam212, consistent with the cDNA being identified in mouse keratinocytes.

Mammalian Expression

To express KS2, the extracellular domain was fused to the amino terminus of the constant domain of immunoglobulinG (Fc) that had a C-terminal 6xHistidine tag. This was performed by cloning polynucleotides 20-664 of KS2 (SEQ ID NO: 273), encoding amino acids 1-215 of polypeptide KS2 (SEQ ID NO: 347), into the mammalian expression vector pcDNA3 (Invitrogen, NV Leek, Netherlands), to the amino terminus of the constant domain of immunoglobulinG (Fc) that had a C-terminal 6xHistidine tag. This construct was transformed into competent XL1-Blue *E. coli* as described in Sambrook et al., *Ibid.* The Fc fusion construct of KS2a was expressed by transfecting Cos-1 cells in 5 x T175 flasks with 180 μg of KS1a using DEAE-dextran. The supernatant was harvested after seven days and passed over a Ni-NTA column. Bound KS2a was eluted from the column and dialysed against PBS.

The ability of the Fc fusion polypeptide of KS2a to inhibit the IL-2 induced growth of concanavalin A stimulated murine splenocytes was determined as follows. A single cell suspension was prepared from the spleens of BALB/c mice and washed into DMEM (GIBCO-BRL) supplemented with 2 mM L-glutamine, 1 mM sodium pyruvate, 0.77 mM L-asparagine, 0.2 mM L-arganine, 160 mM penicillin G, 70 mM dihydrostreptomycin sulfate, 5 x 10^{-2} mM beta mercaptoethanol and 5% FCS (cDMEM). Splenocytes (4 x 10^6/ml) were stimulated with 2 ug/ml concanavalin A for 24 hrs at 37°C in 10% CO_2. The cells were harvested from the culture, washed 3 times in cDMEM and resuspended in cDMEM supplemented with 10 ng/ml rhuIL-2 at 1 x 10^5 cells/ml. The assay was performed in 96 well round bottomed plates in 0.2 ml cDMEM. The Fc fusion polypeptide of KS2a, PBS, LPS and BSA were titrated into the plates and 1 x 10^4 activated T cells (0.1 ml) were added to each well. The plates were incubated for 2 days in an atmosphere containing 10% CO_2 at 37^0C. The degree of proliferation was

determined by pulsing the cells with 0.25 uCi/ml tritiated thymidine for the final 4 hrs of culture after which the cells were harvested onto glass fiber filtermats and the degree of thymidine incorporation determined by standard liquid scintillation techniques. As shown in Fig. 6, the Fc fusion polypeptide of KS2a was found to inhibit the IL-2 induced growth of concanavalin A stimulated murine splenocytes, whereas the negative controls PBS, BSA and LPS did not.

This data demonstrates that KS2 is expressed in skin keratinocytes and inhibits the growth of cytokine induced splenocytes. This suggests a role for KS2 in the regulation of skin inflammation and malignancy.

Example 7

Characterization of KS3

KS3 encodes a polypeptide of 40 amino acids (SEQ ID NO: 129). KS3 contains a signal sequence of 23 amino acids that would result in a mature polypeptide of 17 amino acids (SEQ ID NO: 348; referred to as KS3a).

KS3a was prepared synthetically (Chiron Technologies, Victoria, Australia) and observed to enhance transferrin-induced growth of the rat intestinal epithelial cells IEC-18 cells. The assay was performed in 96 well flat-bottomed plates in 0.1 ml DMEM (GIBCO-BRL Life Technologies) supplemented with 0.2% FCS. KS3a (SEQ ID NO: 348), apo-Transferrin, media and PBS-BSA were titrated either alone, with 750 ng/ml Apo-transferrin or with 750 ng/ml BSA, into the plates and 1 $x10^3$ IEC-18 cells were added to each well. The plates were incubated for 5 days at 37^0C in an atmosphere containing 10% CO_2. The degree of cell growth was determined by MTT dye reduction as described previously (*J. Imm. Meth.* 93:157-165, 1986). As shown in Fig. 7, KS3a plus Apo-transferrin was found to enhance transferrin-induced growth of IEC-18 cells, whereas KS3a alone or PBS-BSA did not, indicating that KS3a and Apo-transferrin act synergistically to induce the growth of IEC-18 cells.

This data indicates that KS3 is epithelial derived and stimulates the growth of epithelial cells of the intestine. This suggests a role for KS3 in wound healing, protection from radiation- or drug-induced intestinal disease, and integrity of the epithelium of the intestine.

SEQ ID NOS: 1-409 are set out in the attached Sequence Listing. The codes for polynucleotide and polypeptide sequences used in the attached Sequence Listing confirm to WIPO Standard ST.25 (1988), Appendix 2.

All references cited herein, including patent references and non-patent references, are hereby incorporated by reference in their entireties.

Although the present invention has been described in terms of specific embodiments, changes and modifications can be carried out without departing from the scope of the invention which is intended to be limited only by the scope of the appended claims.

We claim:

1. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of: (1) the sequences recited in SEQ ID NO: 1-119, 198-274, 349-372, and 399-405; (2) complements of the sequences recited in SEQ ID NO: 1-119, 198-274, 349-372, and 399-405; (3) reverse complements of the sequences recited in SEQ ID NO: 1-119, 198-274, 349-372, and 399-405; (4) reverse sequences of the sequences recited in SEQ ID NO: 1-119, 198-274, 349-372, and 399-405; (5) sequences having at least a 99% probability of being the same as a sequence selected from any of the sequences in (1)-(4), above, as measured by the computer algorithm BLASTP using the running parameters described above; and (6) nucleotide sequences having at least 50% identity to any of the sequences in (1)-(4), above, as measured by the computer algorithm BLASTP using the running parameters and identity test defined above.

2. An expression vector comprising an isolated polynucleotide of claim 1.

3. A host cell transformed with an expression vector of claim 2.

4. An isolated polypeptide comprising an amino acid sequence selected from the group consisting of: (1) sequences provided in SEQ ID NO: 120-197, 275-348, 373-398, and 406-409; (2) sequences having at least a 99% probability of being the same as a sequence of SEQ ID NO: 120-197, 275-348, 373-398, and 406-409, as measured by the computer algorithm BLASTP using the running parameters described above; and (3) sequences having at least 50% identity to a sequence provided in SEQ ID NO: 120-197, 275-348, 373-398, and 406-409, as measured by the computer algorithm BLASTP using the running parameters and identity test defined above.

5. An isolated polynucleotide encoding a polypeptide of claim 4.

6. An expression vector comprising an isolated polynucleotide of claim 5.

7. A host cell transformed with an expression vector of claim 6.

8. An isolated polypeptide comprising at least a functional portion of a polypeptide having an amino acid sequence selected from the group consisting of: (1) sequences provided in SEQ ID NO: 120-197, 275-348, 373-398, and 406-409; (2) sequences having at least a 99% probability of being the same as a sequence of SEQ ID NO: 120-197, 275-348, 373-398, and 406-409, as measured by the computer algorithm BLASTP using the running parameters described above; and (3) sequences having at least 50% identity to a sequence provided in SEQ ID NO: 120-197, 275-348, 373-398, and 406-409, as measured by the computer algorithm BLASTP, using the running parameters and identity test defined above.

9. A method for stimulating keratinocyte growth and motility in a patient, comprising administering to the patient a composition comprising an isolated polypeptide, the polypeptide comprising an amino acid sequence of claim 4.

10. The method of claim 9, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of: (1) a sequence provided in SEQ ID NO: 187, 196, 342, 343, 397 and 398; (2) sequences having at least about 50% identity to a sequence of SEQ ID NO: 187, 196, 342, 343, 397 and 398 as measured by the computer algorithm BLASTP, using the running parameters and identity test defined above.

11. A method for inhibiting the growth of cancer cells in a patient, comprising administering to the patient a composition comprising an isolated polypeptide, the polypeptide comprising an amino acid sequence of claim 4.

12. The method of claim 11, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of: (1) a sequence provided in SEQ ID NO: 187, 196, 342, 343, 397 and 398; and (2) sequences having at least 50% identity to a sequence of SEQ ID NO: 187, 196, 342, 343, 397, and 398, as measured by the computer algorithm BLASTP, using the running parameters and identity test defined above.

13. A method for modulating angiogenesis in a patient, comprising administering to the patient a composition comprising an isolated polypeptide, the polypeptide comprising an amino acid sequence of claim 4.

14. A method of claim 13, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of: (1) a sequence provided in SEQ ID NO: 187, 196, 342, 343, 397 and 398; and (2) sequences having at least 50% identity to a sequence of SEQ ID NO: 187, 196, 342, 343, 397 and 398 as measured by the computer algorithm BLASTP, using the running parameters and identity test defined above.

15. A method for inhibiting angiogenesis and vascularization of tumors in a patient, comprising administering to a patient a composition comprising an isolated polypeptide, the polypeptide comprising an amino acid sequence of claim 4.

16. The method of claim 15, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of: (1) a sequence provided in SEQ ID NO: 187, 196, 342, 343, 397, and 398; and (2) sequences having at least 50% identity to a sequence of SEQ ID NO: 187, 196, 340, 342-346, 397, and 398, as measured by the computer algorithm BLASTP, using the running parameters and identity test defined above.

17. A method for modulating skin inflammation in a patient, comprising administering to the patient a composition comprising an isolated polypeptide, the polypeptide comprising an amino acid sequence of claim 4.

18. The method of claim 17, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of: (1) a sequence provided in SEQ ID NO: 338 and 347; and (2) sequences having at least 50% identity to a sequence of SEQ ID NO: 338 and 347 as measured by the computer algorithm BLASTP, using the running parameters and identity test defined above.

19. A method for stimulating the growth of epithelial cells in a patient, comprising administering to the patient a composition comprising an isolated polypeptide, the polypeptide comprising an amino acid sequence of claim 4.

20. The method of claim 19, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of: (1) a sequence provided in SEQ ID NO: 129 and 348; and (2) sequences having at least 50% identity to a sequence of SEQ ID NO: 129 and 348 as measured by the computer algorithm BLASTP, using the running parameters and identity test defined above.

21. A method for inhibiting the binding of HIV-1 to leukocytes in a patient, comprising administering to the patient a composition comprising an isolated polypeptide, the polypeptide comprising an amino acid sequence of claim 4.

22. A method of claim 21, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of: (1) a sequence provided in SEQ ID NO: 340, 344, 345 and 346; (2) sequences having at least 50% identity to a sequence of SEQ ID NO: 340, 344, 345 and 346 as measured by the computer algorithm BLASTP, using the running parameters and identity test defined above.

23. A method for treating an inflammatory disease in a patient, comprising administering to the patient a composition comprising an isolated polypeptide, the polypeptide comprising an amino acid sequence of claim 4.

24. The method of claim 23, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of: (1) a sequence provided in SEQ ID NO: 340, 344, 345 and 346; and (2) sequences having at least 50% identity to a sequence of SEQ ID NO: 340, 344, 345 and 346 as measured by the computer algorithm BLASTP, using the running parameters and identity test defined above.

25. A method for treating cancer in a patient, comprising administering to the patient a composition comprising an isolated polypeptide, the polypeptide comprising an amino acid sequence of claim 4.

26. The method of claim 25, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of: (1) a sequence provided in SEQ ID NO: 340, 344, 345 and 346; and (2) sequences having at least 50% identity to a sequence of SEQ ID NO: 340, 344, 345 and 346 as measured by the computer algorithm BLASTP, using the running parameters and identity test defined above.

27. A method for treating neurological disease in a patient, comprising administering to the patient a composition comprising an isolated polypeptide, the polypeptide comprising an amino acid sequence of claim 4.

28. The method of claim 27, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of: (1) a sequence provided in SEQ ID NO: 187, 196, 340, 342-346, and 395; and (2) sequences having at least 50% identity to a sequence of SEQ ID NO: 187, 196, 340, 342-346, and 395, as measured by the computer algorithm BLASTP, using the running parameters and identity test defined above.

Figure 1

Distribution of human TAK1 mRNA in human tissues

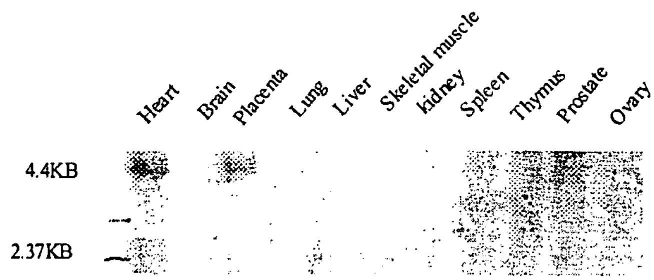


Figure 2

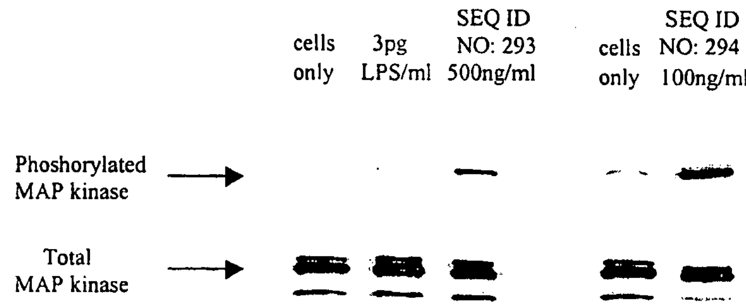

cells only
3pg LPS/ml
SEQ ID NO: 293 500ng/ml
cells only
SEQ ID NO: 294 100ng/ml
Phoshorylated MAP kinase
Total MAP kinase

Figure 3

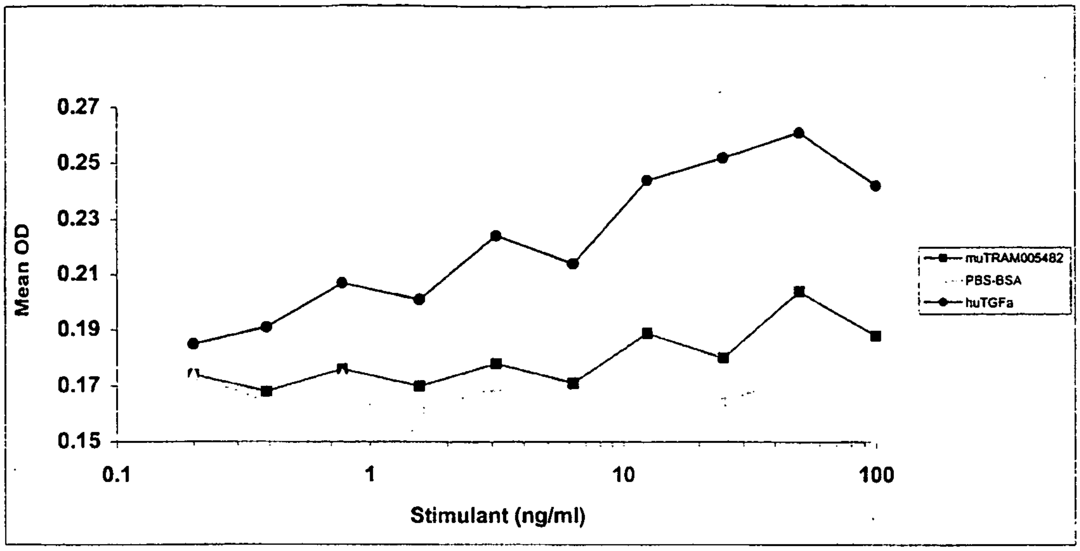

0.27
0.25
0.23
0.21
0.19
0.17
0.15
Mean OD
0.1
1
10
100
Stimulant (ng/ml)
muTRAM005482
PBS-BSA
huTGFa

Figure 4

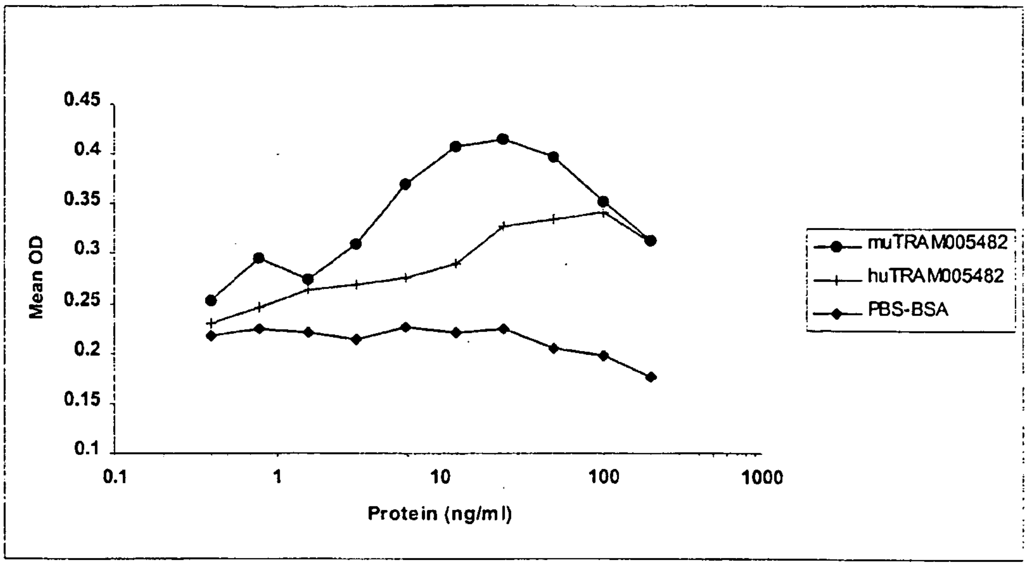

0.45
0.4
0.35
0.3
0.25
0.2
0.15
0.1
Mean OD
0.1
1
10
100
1000
Protein (ng/ml)
muTRAM005482
huTRAM005482
PBS-BSA

Figure 5

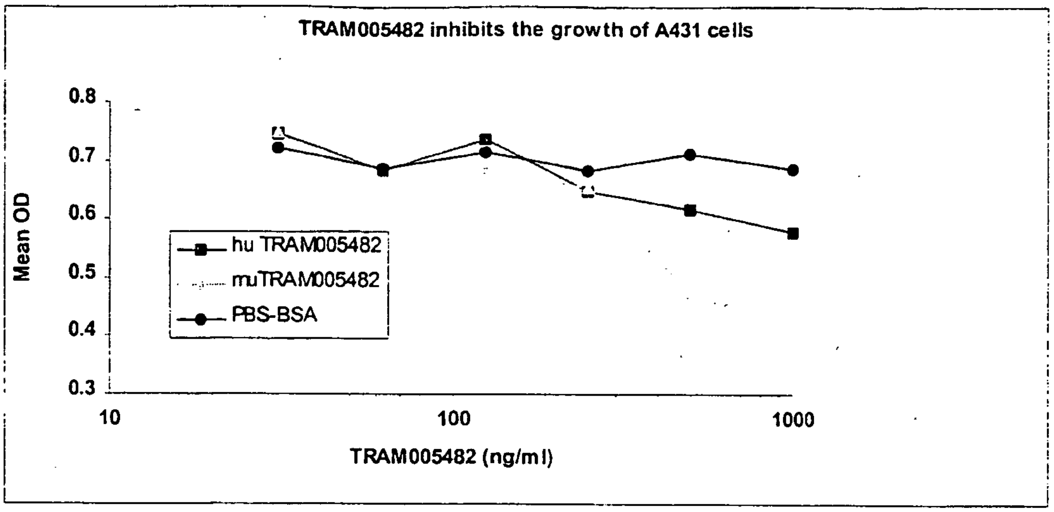

TRAM005482 inhibits the growth of A431 cells
Mean OD
0.8
0.7
0.6
0.5
0.4
0.3
10
100
1000
TRAM005482 (ng/ml)
hu TRAM005482
muTRAM005482
PBS-BSA

Figure 6

Key: Br, Brain; Th,Thymus; Sk, Skin; Ht, Heart; Lg, Lung; Spl, Spleen; Sth, Stomach; Kdy, Kidney; Lr, Liver; LI, Lower intestine; Ts, Testis; Mle, Muscle.

Br Th Sk Ht Lg Spl Sth Kdy Lr LI Mle

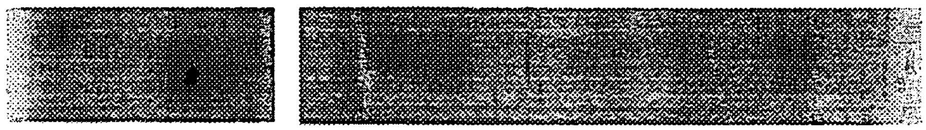
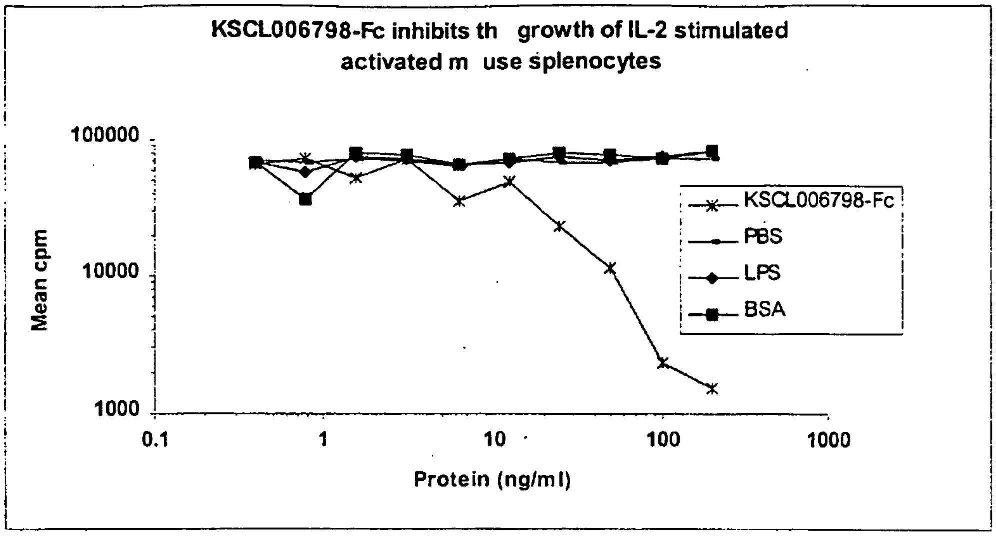


Figure 7


KSCL006798-Fc inhibits th growth of IL-2 stimulated activated m use splenocytes
100000
10000
1000
Mean cpm
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1
10
100
1000
Protein (ng/ml)
KSCL006798-Fc
PBS
LPS
BSA

Figure 8

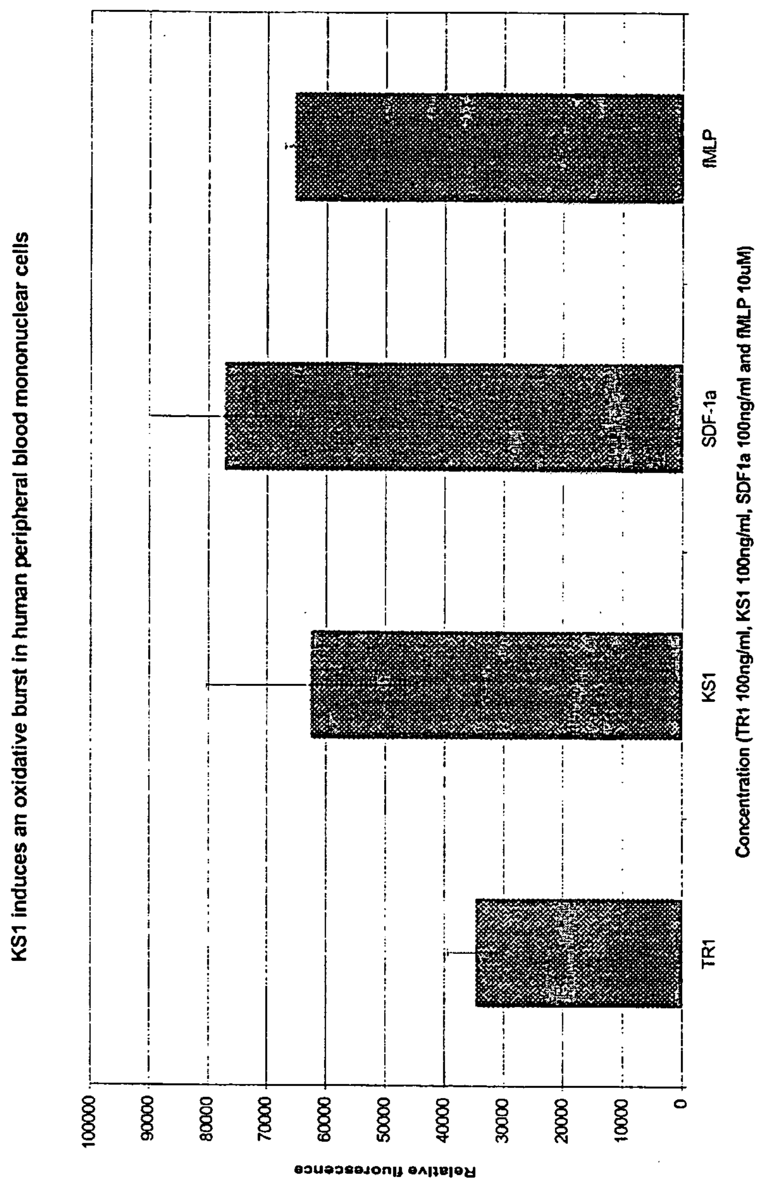

KS1 induces an oxidative burst in human peripheral blood mononuclear cells
Relative fluorescence
100000
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
TR1
KS1
SDF-1a
fMLP
Concentration (TR1 100ng/ml, KS1 100ng/ml, SDF1a 100ng/ml and fMLP 10uM)

Figure 9

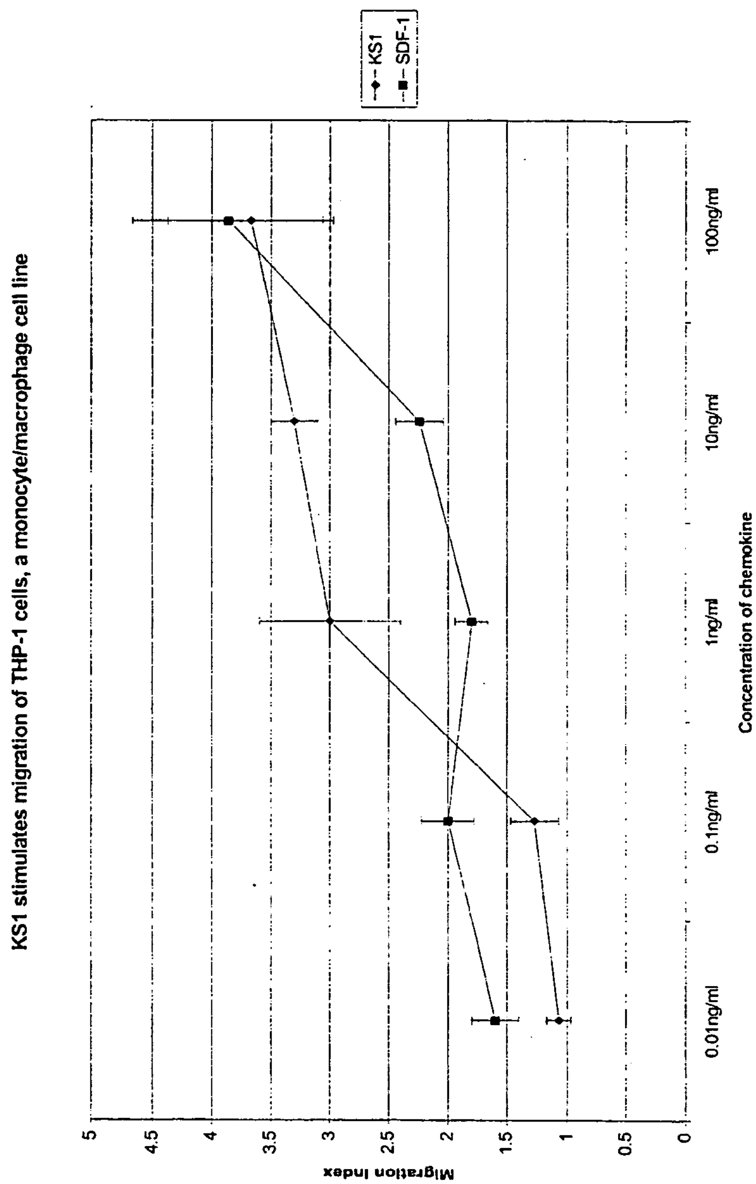
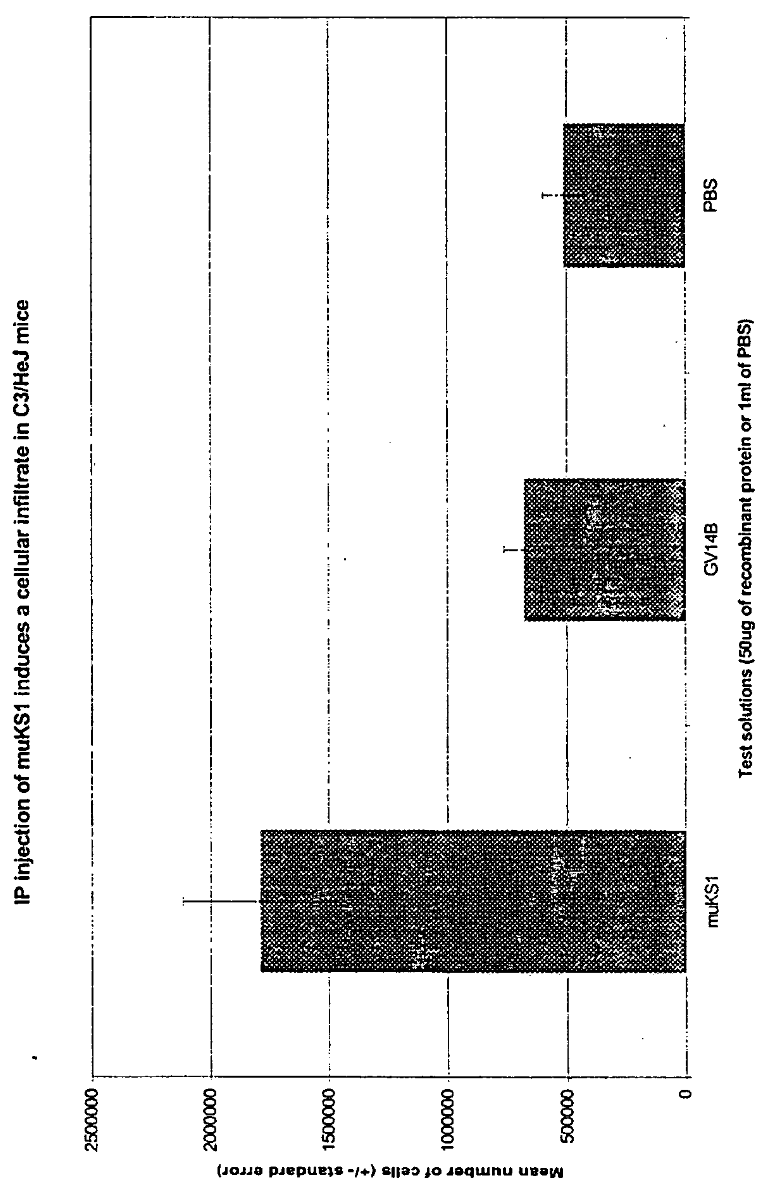

KS1 stimulates migration of THP-1 cells, a monocyte/macrophage cell line
KS1
SDF-1
Migration Index
5
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
0.01ng/ml
0.1ng/ml
1ng/ml
10ng/ml
100ng/ml
Concentration of chemokine

Figure 10


IP injection of muKS1 induces a cellular infiltrate in C3/HeJ mice
Mean number of cells (+/- standard error)
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2000000
1500000
1000000
500000
0
muKS1
GV14B
PBS
Test solutions (50ug of recombinant protein or 1ml of PBS)

Figure 11

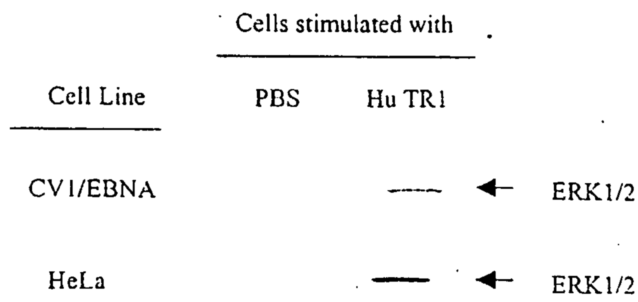

Cells stimulated with
Cell Line
PBS
Hu TR1
CV1/EBNA
ERK1/2
HeLa
ERK1/2

Figure 12

mu and huTR1 upregulate huTR1 mRNA expression in HeLa cells

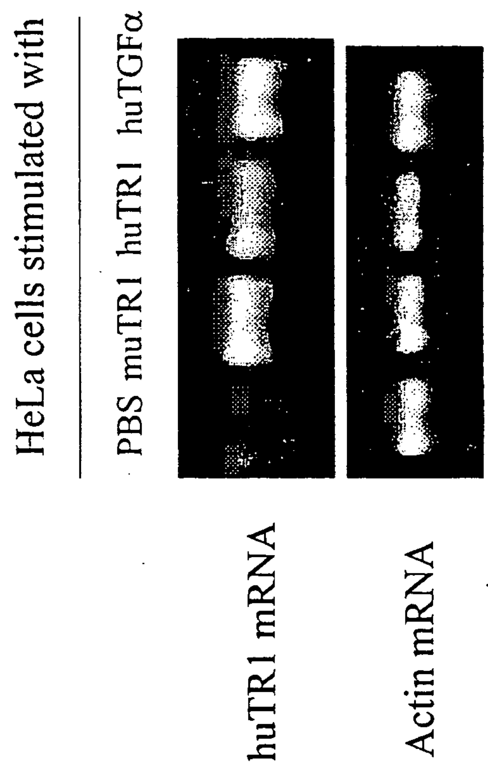


Figure 13A

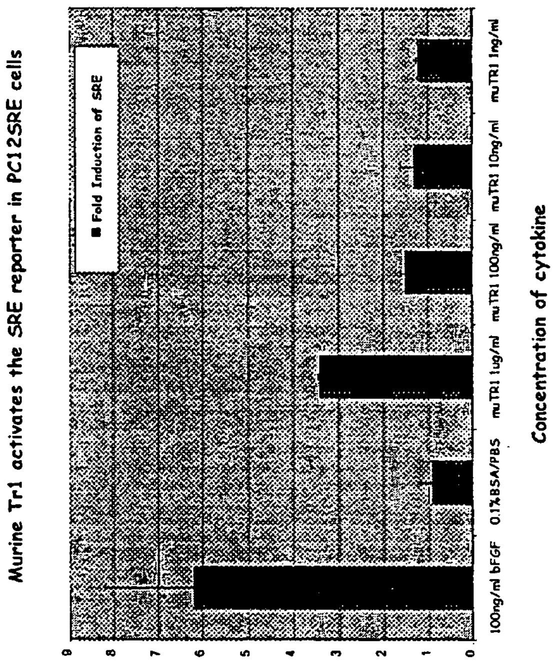


Figure 13B

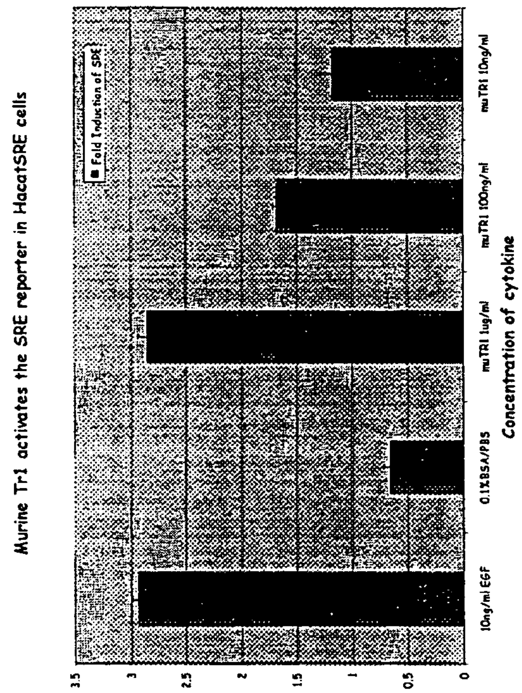
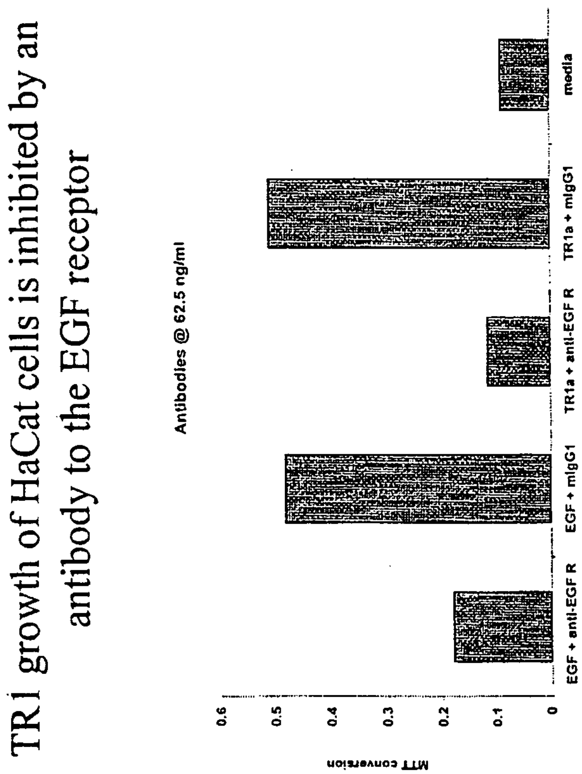


Figure 14


TR1 growth of HaCat cells is inhibited by an antibody to the EGF receptor
Antibodies @ 62.5 ng/ml
MTT conversion
0.6
0.5
0.4
0.3
0.2
0.1
0
EGF + anti-EGF R
EGF + mIgG1
TR1a + anti-EGF R
TR1a + mIgG1
media

SEQUENCE LISTING

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Strachan, Lorna
Sleeman, Matthew
Onrust, Rene
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Kumble, Anand

<120> Compositions isolated from skin cells
and methods for their use

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<210> 11
<211> 969
<212> DNA
<213> mouse

<400> 11
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<211> 1411
<212> DNA
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<400> 12
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<211> 888
<212> DNA
<213> mouse

<400> 13
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<211> 547
<212> DNA
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<400> 14
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<210> 15
<211> 318
<212> DNA
<213> Rat

<400> 15
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<210> 16
<211> 856
<212> DNA
<213> Rat

<400> 16
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<210> 17
<211> 349
<212> DNA
<213> Rat

<400> 17
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<210> 18
<211> 1057
<212> DNA
<213> Rat

<220>

<400> 18
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<210> 19
<211> 750
<212> DNA
<213> Rat

<400> 19

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<210> 20
<211> 849
<212> DNA
<213> Rat

<400> 20

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<210> 21
<211> 312
<212> DNA
<213> Human

<400> 21

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<210> 22
<211> 1023
<212> DNA
<213> mouse

<400> 22
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<210> 23
<211> 997
<212> DNA
<213> mouse

<400> 23
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<210> 24
<211> 529
<212> DNA
<213> Rat

<400> 24
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<210> 25
<211> 1230
<212> DNA
<213> Rat

<400> 25

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aagtacactt tctgcagctg gcgcccgcca ggctgctacc gagctgcgcg ctcttccagg     1140
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<210> 26
<211> 393
<212> DNA
<213> Rat

<400> 26

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ctgggagagc tggggagccg ggaagggcct acagactaca agagaggatc ctggcgtctg      180
ggcctcctgg gtcatcacca tgaggccact tcttgccctg ctgcttctgg gtctggcatc      240
aggctctcct cctctggacg acaacaagat ccccagcctg tgtcccgggc agcccggcct      300
cccaggcaca ccaggccacc acggcagcca aggcctgcct ggccgtgacg gcctgatggc      360
cgcgacggtg cacccggagt ccgggagaga aac                                   393
```

<210> 27
<211> 778
<212> DNA
<213> Rat

<400> 27

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ctgcaggtcg acactagtgg atccaaagat tcggcacgag ataaggcaca tttgcttcat       60
aaaataaaaa aaaaggaaat ttacttagcc gcatgtcagt cacccaaatt ttgagtgtac      120
aaatgaaatg gaaaacattt attacacaaa tttaattaca attctaggga ataaacatgc      180
aaatcagatg gagctcaatc tgcaggcgct gatcctctcc ccctggtttg cagtctgtgc      240
acctcctgga ttcgcccgcg accaggcagt cagaggcctg gctcttgcag gcaggaggat      300
cactgttgta aagaacagcg tcacatttag cgcatctggc gtagtagcag tttttaacac      360
tttgcgcagg tgcctccctt cccccacccg cgctttgtta ggtctacctc tctaaatctc      420
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```
tgccttcctc gcacagtaag tgacctctcc atgacaaagg gcccccagac agcagttata      480
aatcaatgtg ttttgggttt gtttgtttgt ttgttttgtt ttaaagaaaa acccggccat      540
gcttggtggc acttgccttt aatagtagcg cttggtagac agaggcaagc ggttctctgt      600
aagttcaagg ccagcctggt ctacacagtg agaccgggtc tcaaaaacaa aacaacaaaa      660
aacaactcct attgaatcca ctacaggaag ggggggcgcg gatcactgtc tgcaaactaa      720
agtgacttga gctcctgtca cagcctttcc agcaagggca agcttcttta ttagttat        778
```

<210> 28
<211> 1123
<212> DNA
<213> Rat

<400> 28

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cgggtgccta cagcccccat cagcttcccc ggggagattc tgccgatttg tcacgagcca      180
tgctcaggag gcagctcgtc tggtggcacc tgctggcttt gcttttcctc ccattttgcc      240
tgtgtcaaga tgaatacatg gagtctccac aagctggagg actgccccca gactgcagca      300
agtgttgcca tggagattat ggattccgtg gttaccaagg gcccccctgga cccccaggtc     360
ctcctggcat tccaggaaac catggaaaca atggaaataa cggagccact ggccacgaag      420
gggccaaggg tgagaaagga gacaaaggcg acctggggcc tcgaggggaa cgggggcagc      480
atggccccaa aggatagaag ggatacccag gggtgccacc agagctgcag attgcgttca      540
tggcttctct agcgactcac ttcagcaatc agaacagtgg cattatcttc agcagtgttg      600
agaccaacat tggaaacttc ttcgatgtca tgactggtag atttggggcc cccgtatcag      660
gcgtgtattt cttcaccttc agcatgatga agcatgagga cgtggaggaa gtgtatgtgt      720
accttatgca caatggtaac acggtgttca gcatgtacag ctatgaaaca aagggaaaat      780
cagatacatc cagcaaccat gcagtgctga agttggccaa aggagatgaa gtctggctaa      840
gaatgggcaa cggtgccctc catggggacc accagcgctt ctctaccttc gcaggctttc      900
tgctttttga aactaagtga tgaggaagtc aggatagctc catgctaagg gcgatttgta      960
ggtgagctag ggttgttagg atctgagggg tgttggagtt gggcttctct atggagtatt     1020
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<210> 29
<211> 849
<212> DNA
<213> Rat

<400> 29

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tatgcttggg gcaacttcac tatcctggcc ctgggtgctg tgggctgtgg cccagcggga      180
ctctgttgat gccattggca tgtttcttgg tggcttggtt gccaccatct tcctggacat      240
tatctacatt agcatcttct actcaagcgt tgccgttggg gacactggcc gcttcagtgc      300
cggcatggcc atcttcagct tgctgctgca agcccttctc ctgctgcctc gtctaccaca      360
tgcaccgggc agcgaggggg tgagctcccg ctccgctcgg atttcttcgg accttctcag      420
gaacatagtg cctaccagac aattgactcg tcagactcac ctgcagaccc ccttgcaagc      480
ctggagaaca agggccaagc tgcccccccgg gggtactgaa gctgtccctg gccgtcctgg     540
ggcccagcag gatgcttgtc accttcttta ctggacctac aatggggtat cctccattcc      600
ctgccacaga ggtggcctga gtcatgtgcc ctcggaggtc ccagctgaga agagcccagt      660
cctaattctc catgctgccc ctccattcaa gacacctgtt aacccctggg ctagaactgt      720
ggttggtttc ttcccctcct ccccatcact ataacacaca accgccgagc tgtgcagagt      780
gttcagggcc atccaggcct tatgggccaa tgatcactgc ctctcaggct accccaaggt      840
gacccagcc                                                              849
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<210> 30
<211> 1015
<212> DNA
<213> Rat

<220>

<400> 30
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caaagcgagc agctgggaga gctggggagc cgggaagggc ctacagacta caagagagga 180
tcctggcgtc tgggcctcct gggtcatcac catgaggcca cttcttgccc tgctgcttct 240
gggtctggca tcaggctctc ctcctctgga cgacaacaag atccccagcc tgtgtcccgg 300
gcagcccggc ctcccaggca caccaggcca ccacggcagc caaggcctgc ctggccgtga 360
cggccgtgat ggccgcgacg gtgcacccgg agctccggga gagaaaggcg agggcgggag 420
accgggacta cctgggccac gtggggagcc cgggccgcgt ggagaggcag gacctgtggg 480
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caatgagcag ggacattacg atgccactac cggcaagttc acctgccaag tgcctggtgt 660
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gctctcaggg ggtgcgatgg tgaggctaga acctgaggac caggtatggg ttcaggtggg 840
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<210> 31
<211> 452
<212> DNA
<213> Human

<400> 31
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tgcgacacac ataattgtcc caatttttaa gattgatggg gagcatgaag catttttta 180
atgtgttggc aggccccatt aaatgcataa actgcatagg actcatgtgg tctgaatgta 240
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tctgagtgag ctaactgaca caatgaaact gtcaggcatg tttctgctcc tctctctggc 360
tcttttctgc tttttaacag gtgtcttcag tcagggagga caggttgact gtggtgagtc 420
caggacacca aggcctactg cactcgggaa cc 452

<210> 32
<211> 434
<212> DNA
<213> mouse

<400> 32
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attgttaaaa aattgacatc agaaatattt acagaaatag atacctgttt gaataaagtt 120
agagatgaaa tttttgctaa acttcaaccg aagcttagat gcacattagg tgacatggaa 180
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tgtgtgaaga gtctggtcac ctttaccaat attgttcctg agtggcatcc actcaatgct 360
gcccattttg gtccatgtaa cagctgcaac agtaaatcac aaataagaaa aatggtgttg 420
gaaagagcgt cgcc 434

<210> 33
<211> 903
<212> DNA
<213> mouse

<400> 33
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ccctgggccc aatggtcaca gtcacctgct gaagacccca ctgggtggcc agaaacgcag 120
tttttcccac ctgctgccct cacctgagcc cagcccagag ggcagctacg tggccagca 180
ctcccagggc ctcggcggcc actacgcgga ctcctacctg aagcggaaga ggattttcta 240
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cgtcactcct gtgttctggc ctcttgagtg cctttggagg tgtctctgac ctgtgaggat 600
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cct 903

<210> 34
<211> 1359
<212> DNA
<213> mouse

<220>
<221> unsure
<222> (644)...(644)

<400> 34
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gctcttttta aaagtttgaa aaaaaaaaaa aaaaactcg 1359

<210> 35
<211> 797
<212> DNA
<213> mouse

<400> 35
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aagaagtacc agctgaacct gccatcttac cctgacacag agtgtgtcta ccgtctacag 720
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aaaaaaaaaa aaactcg 797

<210> 36
<211> 896
<212> DNA
<213> mouse

<400> 36
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<210> 37
<211> 501
<212> DNA
<213> mouse

<400> 37
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cagcatcgtt cttatatgcg actaacagaa aaggaagatg aatcattacc aatagatata 180
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gcaacaaatt cttcaaacct agatgcattg tcctctaata catcgttgaa gttacgaaag 420
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agtattggag tttggggtgt a 501

<210> 38
<211> 766
<212> DNA
<213> mouse

<400> 38
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cggcggcat cccccggccg ccgcacgcac aggccggcgc cctccttgcc tccctgctcc 180
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tacaagtggc tttttgctgg gcggttggcg gggggcgggg ggacct                766

      &lt;210&gt; 39
      &lt;211&gt; 480
      &lt;212&gt; DNA
      &lt;213&gt; mouse

      &lt;400&gt; 39
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      &lt;210&gt; 40
      &lt;211&gt; 962
      &lt;212&gt; DNA
      &lt;213&gt; mouse

      &lt;400&gt; 40
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cattcatctc tctctcattc ccctgctctg catcctgatg agaaactgtt tggcttttaa    120
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aatgagtggt ttgcagtgaa agccaggcat cctgtagttt ccatcccctc cccatccca    900
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aa                                                                  962

      &lt;210&gt; 41
      &lt;211&gt; 794
      &lt;212&gt; DNA
      &lt;213&gt; mouse

      &lt;400&gt; 41
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cgggctcgcg cctgccacgg gtcatcagcc agcagagtgt gtgtcgtgca aggcccatct    120
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gaggtgggta ggcaggattc tcaataaaga cttggtactt tctgtcttga aaaaaaaaaa    780
aaaaaaaact cgag                                                     794
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<210> 42
<211> 1152
<212> DNA
<213> mouse

<400> 42
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caggctgggc cacaggaagc tgctgactgg ccacttgaca ccctccccct aaagctaatg    120
tctgtgacta tagggaggtt agcacttttt ctaattggaa ttcttctctg tcctgtggcc    180
ccatccctca cccgctcttg gcctggacca gatacatgca gcctctttct ccagcacagc    240
ctttccctga gcctgaggtt agggcagagt ttagagggtg ggctaagtgt atgttttcat    300
gtatgcattc atgcctgtga gtgtgtggct tgctgtcgtg tcctctggga tcccaagcca    360
cgcgggtctt ccctctgtag atgggtcctg ggttctatca cctgcttatt tatgtacgag    420
gttgggggt ggacccaggg tgggttgatt gtctctttgt aaggaagtat gtgtcggggg    480
tgacacgagg ctaagcccga gaaaccccgg gagacagcac tgcataagaa actggtttcc    540
magactgcag agggagctgc acttttgttt tgaccaaaaa caaaaaacaa aacaaaacaa    600
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acacaggtga cagtcccaag tagataacct ccatgggaca agttgggtgt tgccttaccc   1140
gcctgcccag cc                                                       1152
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<210> 43
<211> 446
<212> DNA
<213> mouse

<400> 43
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ccaggtcctc tggagaaata accagtgctc ttaaccacta agccatctca acagccccaa    240
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ctaatataga ttatttatga attcaggtgg cttaatggta tatgcatgaa ttagtagtaa    360
aacaagaact agggccagca agtggcttaa gggtgcctgc taaccatctc agccacctga    420
gttcagtctc caggaaccac acagtg                                         446
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<210> 44
<211> 391
<212> DNA
<213> mouse

<400> 44
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tctgccacgt ctgctttgga cacttcaaat acctcagtgc ccacaactac aagattgaac    120
acacagagac agatgccgtg agctccagaa gtaatggacg gccccccact gctggcgctg    180
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gagatggggc tcctgggagc tcaggcgatg agccccccatc gtcctcctcc caagacgagg    300
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tcatagagaa tgagattcac cagtaagggg t                                   391
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<210> 45
<211> 516
<212> DNA
<213> Rat

<400> 45
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cccggcctcc ttcctggagg aagtggcggg cagtggggaa gctgagggtt cttcagcctc 120
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ctctttcccc gaaaagaagt atgtggacca gagagaccgg gctgggggc cccatgcctt 420
cagcgaggtc cctgacaggg cacctgacag ccggcaggaa gagggcctgg acttcttcca 480
gcagctccag gctgacattc tggcttgcta ctcaga 516

<210> 46
<211> 306
<212> DNA
<213> mouse

<400> 46
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agggggatca gaaatggggt ctcccatttc tggtgtctgc ccagtccttc caggtgggct 180
cttcgtagcc ctggggtgga ttttcctcct cttccacaga gatgcttttt ctctgcatac 240
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ccccag 306

<210> 47
<211> 439
<212> DNA
<213> mouse

<400> 47
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gcacatatta ctgagccatt gcaagcaatg ggaggggtcc acaatgacac acacacacac 180
acacacacac atacacatac acacaccccc gagacagtgc cagagctaac agcctacatg 240
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ttgcaagtga tcttccatgc agtatgaaac atgcagacag cactggagtg tggcaagagt 360
gagcttgccc cacaagtctc tcggggatgt tgtactcttg tgtgtgttta cagtatcatg 420
gctgttacat ctactggtc 439

<210> 48
<211> 159
<212> DNA
<213> mouse

<220>
<221> unsure
<222> (3)...(3)

<400> 48
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ttactgagcc attgcaagca atgggagggg tccacaatg 159

<210> 49
<211> 465
<212> DNA
<213> Rat

<400> 49
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ttcactggct gttgacaacc tggggctgct tggcgttctc aggctcctat gcttggggca 120
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gagggggtga gctcccgctc cgctcggatt tcttcggacc ttctcaggaa catagtgcct 420
accagacaat tgactcgtca gactcacctg cagaccccct tgcaa 465

<210> 50
<211> 337
<212> DNA
<213> Rat

<220>

<400> 50
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tctacctcct cctcggggc ttctccttct gcnaagttcg tctcaataag cgcaaggaat 300
acatggtgcg ctagagcgna gtccnactct ccccatt 337

<210> 51
<211> 371
<212> DNA
<213> Rat

<220>
<221> unsure
<222> (80)...(80)

<221> unsure
<222> (312)...(312)

<221> unsure
<222> (319)...(319)

<221> unsure
<222> (353)...(354)

<400> 51
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actgtccctg atcttcttcg ccaagtttct gaggaaagct gacgccgacc gacagcgagc 240
aagcctgcct cgctgccagc cttgccctag cgctaaatgg tgtctttacc aacatcataa 300
gactgatagt gngcaaggnc acgcccaaat tgcttctacc gagtgttccc cgnncgggat 360
tgcccattct t 371

<210> 52
<211> 228
<212> DNA
<213> Rat

<400> 52
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gagagtcatc actgacaaca gagatggacc agtacagaat tacctgct 228

<210> 53
<211> 361
<212> DNA
<213> Human

<400> 53
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cattgtgctt aataatacca agactaagca ccataaccaa gaaatactaa tgtaaagatt 300
gtttcttgtt tcaggaatgg ttaattcttc aacgttggta tgataatgat aacttgtttt 360
g 361

<210> 54
<211> 403
<212> DNA
<213> Human

<220>

<400> 54
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aagtccgtga cacgggaaga cactgggaca tacacttgta tgg 403

<210> 55
<211> 413
<212> DNA
<213> Human

<400> 55
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<210> 56
<211> 452
<212> DNA
<213> Human

<400> 56
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<210> 57

<211> 190
<212> DNA
<213> Rat

<220>

<400> 57
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cagtgtgcaa catatataaa acagaaatac taactctaca ggcagtatgt cgacgcggcc 180
gcgtattcgg 190

<210> 58
<211> 413
<212> DNA
<213> mouse

<400> 58
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<210> 59
<211> 325
<212> DNA
<213> mouse

<220>
<221> unsure
<222> (213)...(213)

<221> unsure
<222> (223)...(223)

<221> unsure
<222> (227)...(227)

<221> unsure
<222> (243)...(243)

<400> 59
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agagagggag tgaagaaagg ggcca 325

<210> 60
<211> 372
<212> DNA
<213> mouse

<400> 60
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tggctgtgtg ga 372

<210> 61
<211> 363
<212> DNA
<213> mouse

<220>
<221> unsure
<222> (15)...(15)

<400> 61
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taa 363

<210> 62
<211> 399
<212> DNA
<213> mouse

<400> 62
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<210> 63
<211> 399
<212> DNA
<213> mouse

<220>

<400> 63
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<210> 64
<211> 2481
<212> DNA
<213> Rat

<400> 64
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<210> 65
<211> 3008
<212> DNA
<213> mouse

<220>
<400> 65

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<210> 66
<211> 1888
<212> DNA
<213> mouse

<220>
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<221> unsure
<222> (1755)...(1755)

<221> unsure
<222> (1864)...(1864)

<400> 66

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```

<210> 67
<211> 1260
<212> DNA
<213> Rat

<400> 67

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<210> 68
<211> 1729
<212> DNA
<213> mouse

<400> 68

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<210> 69
<211> 355
<212> DNA
<213> Rat

<400> 69
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<210> 70
<211> 1421
<212> DNA
<213> Human

<400> 70
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<210> 71
<211> 378
<212> DNA
<213> Human

<400> 71
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<210> 72
<211> 267
<212> DNA
<213> mouse

<400> 72
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<210> 73
<211> 1633
<212> DNA
<213> mouse

<220>

<400> 73
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<210> 74
<211> 1252
<212> DNA
<213> mouse

<400> 74
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<210> 75
<211> 2411
<212> DNA
<213> mouse

<400> 75
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<210> 76
<211> 1335
<212> DNA
<213> mouse

<400> 76

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<211> 440
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<213> mouse

<220>

<400> 77
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<210> 78
<211> 204
<212> DNA
<213> mouse

<400> 78
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cctctgtgtc ctcttcatcc caat 204

<210> 79
<211> 300
<212> DNA
<213> mouse

<220>
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<400> 79
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aacaccttct tctggcctcc atggcacaca gaacccccca acacatgctc atccactctc 180
aaagagacat acataaaaat aaatatttag gtcctgggtc cctcagagac tagtcttcac 240
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<210> 80
<211> 214
<212> DNA
<213> mouse

<400> 80
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<210> 81
<211> 152
<212> DNA
<213> mouse

<220>

<400> 81
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ctgatggagc tgaacggtat cccctaaaag ta 152

<210> 82
<211> 181
<212> DNA
<213> mouse

<220>

<400> 82
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<210> 83
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<212> DNA
<213> mouse

<220>

<400> 83
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<400> 84
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acattgttgg ccgcacagca acgtgctgga cacaagcatg ctctcatccc cagatgtggt 180
gcgcatgctg ctgtccctgc agcccttcct gca 213

<210> 85
<211> 273
<212> DNA
<213> mouse

<220>

<400> 85
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<210> 86
<211> 218
<212> DNA
<213> mouse

<400> 86
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<210> 87
<211> 335
<212> DNA
<213> mouse

<400> 87
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<210> 88
<211> 410
<212> DNA
<213> mouse

<400> 88
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<210> 89
<211> 279
<212> DNA
<213> mouse

<220>

<400> 89
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gacagggtgg agggcattgt ccgacagaac cattgctgt 279

<210> 90
<211> 398
<212> DNA
<213> mouse

<400> 90
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<211> 279
<212> DNA
<213> mouse

<400> 91
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<210> 92
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<212> DNA
<213> mouse

<400> 92
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<210> 93
<211> 339
<212> DNA
<213> mouse

<400> 93
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<210> 94
<211> 55
<212> DNA
<213> mouse

<400> 94
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<210> 95
<211> 186
<212> DNA
<213> mouse

<400> 95
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ggcaga 186

<210> 96
<211> 244
<212> DNA
<213> mouse

<400> 96
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<210> 97
<211> 116
<212> DNA
<213> mouse

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<221> unsure
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<221> unsure
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<210> 98
<211> 307
<212> DNA
<213> mouse

<400> 98
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tgggtgg 307

<210> 99
<211> 360
<212> DNA
<213> mouse

<220>

<400> 99
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<211> 257
<212> DNA
<213> mouse

<400> 100
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<211> 203
<212> DNA
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<400> 101
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<210> 102
<211> 300
<212> DNA
<213> mouse

<400> 102
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<210> 103
<211> 370
<212> DNA
<213> mouse

<220>

<400> 103
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<210> 104
<211> 423
<212> DNA
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<400> 104
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gat 423

<210> 105
<211> 117
<212> DNA
<213> mouse

<400> 105
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<210> 106
<211> 133
<212> DNA
<213> mouse

<400> 106
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<210> 107
<211> 217
<212> DNA
<213> mouse

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<222> (40)...(42)

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<221> unsure
<222> (55)...(58)

<221> unsure
<222> (152)...(152)

<221> unsure

<222> (155)...(155)

<221> unsure
<222> (165)...(165)

<400> 107
nttttttttg ngcgcacnnn nnngnnnncg cccnggnngn nnagcctacn nncannnngt 60
tttcttctcc aggctgaaga cctgaacgtc aagttggaag gggagccttc catgcggaaa 120
ccaaagcagc ggccgcggcc ggagcccctc ancancccca ccaangcggg cactttcatc 180
gcccctcctg tctactccaa catcacccct taccaga 217

<210> 108
<211> 346
<212> DNA
<213> mouse

<220>

<400> 108
gggcatagaa ggcatctcga aaagaatact tatttgaatt gaaggaagat gaagaggcct 60
gcaggaaggc tcagaagaca ggagtgtttt acctctttca tgacctggat cctttgctcc 120
aggcgtcagg acatcgatac ctggtgcccc ggcttagccg agcagagttg gaagggctgc 180
tgggtaagtt cggacaggat tcgcaaagaa ttgaagattc ggtgctggtt gggtgctccg 240
agcagcagga agcatggttt gctttggatc taggtctgaa gagtgcctcc tccagccgtg 300
gacaagtatc gctgctccag cagcttgact gctgtaaaga ggatct 346

<210> 109
<211> 242
<212> DNA
<213> mouse

<400> 109
ccacattgtc cacaactgga aggcacgatg gttcatcctt cggcagaaca cgctcctgta 60
ttacaagcta gagggtggcc ggcgagtaac cccgcccaag gggaggattg tccttgatgg 120
ctgcaccatc acctgcccct gcctggagta tgaaaaccgg ccgctcctca ttaaactgaa 180
gacccgaact tccactgagt acttcctgga agcctgttct cgagaggaga gagactcctg 240
gg 242

<210> 110
<211> 310
<212> DNA
<213> mouse

<220>

<400> 110
cccggccggg aatccaggtg gtagctggtg gagtcgcctc cggagagtga cgcgcagact 60
cggctccccc gcggcccgcc ctcctgccgg cctcgccgcg gtctcccttg ctccctgaga 120
tcgctgagcg ctgagcagcg gcccgggaga ggaggccttg ggcgacgggg cgcggagagg 180
gagggcgggc gggcagtggg ggcgccgcgg atctctatat ggcgacggct ctgtcgggtc 240
tggctgtccg gctgtcgcgc tcggccgnc cgcccgctcc tatggggtct tctgcaa-gg 300
ggctgacccg 310

<210> 111
<211> 228
<212> DNA
<213> mouse

<400> 111
ttctttttta acatttggtg gtttttttct ttactctttt tttcttttcc ttcttttttct 60
gccctcaacc ccccaactcc tttggtatga agtactttta acatttatat ttcattgtta 120

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cactttaaat tttgtaagga aaactctgat atttcattcc tcctgaacca ctaatgttag      180
aatttatttc taagaatcag tcaacatgta tactcttaat agtgaatt                  228

      <210> 112
      <211> 292
      <212> DNA
      <213> mouse

      <400> 112
gtggggtccc agacttgcca accaaagggc cattcctggt atatggttct ggcttcagct       60
ctggtggcat ggactatggt atggttggtg gcaaggaggc tgggaccgag tctcgcttca      120
aacagtggac ctcaatgatg gaagggctgc catctgtggc cacacaagaa gccaccatgc      180
acaaaaacgg cgctatagtg gcccctggta agacccgagg aggttcacca tacaaccagt      240
ttgatataat cccaggtgac acactgggtg gccatacggg tcctgctggt ga              292

      <210> 113
      <211> 255
      <212> DNA
      <213> mouse

      <220>

      <400> 113
ttagatgact taggacttta atgttttcca tgcagtcgat tgaaaacact gatacatgaa       60
caaccagaaa aagacctcag caatgtatag acctggaata tatagtgttg ccctggttaa      120
actacaagaa cagccacgtg atcacagttt gagggtggaa ggcaggggtg tgactgagtt      180
ttgtttaacg gcctaaccga aaagcaaaga atcaaccatt tcttctactt gtggcaagaa      240
acgagagtca tggtg                                                       255

      <210> 114
      <211> 197
      <212> DNA
      <213> mouse

      <400> 114
gacccacatg tgaacagccg cgtgtatgtc acactgctct gtgtgtgatt tcttcacgtg       60
tgcatgtgcg ctcttggtct ttccacttat tgcctcgttc gtaagaaacc aaccataagg      120
tgccaaggag gttttattcc ttttttttt aaagatgaca aatgtacaga tgttagtaca       180
gatgttaatg tacagat                                                     197

      <210> 115
      <211> 205
      <212> DNA
      <213> mouse

      <400> 115
aaaacatttc acaaaacagc aaaacaaaat tgatacaatc aaaaaaacaa cactataacc       60
aacataggtg aaaacagcca aacacataat gtacaatctg gtgttccagg acaaacatct      120
gtcatataca tggtatatac atatatactt tttcactcaa tatattatga caatatatat      180
ttaaaatttt gttatagaca aaaaa                                            205

      <210> 116
      <211> 202
      <212> DNA
      <213> mouse

      <220>

      <400> 116
cctccctcat cctctacttc ccttttcctt cctgcttgat tttctcattc cagaccccta       60
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tgcacacaca cacacacaca cacacacaca cacgaacaca cgcacacaca cacacacacg     120
cacacacaca ctgtccatcc atagttactt atttagtttt ccattcctag agagatctaa     180
tcatccccta gtcagtgcct aa                                              202

      <210> 117
      <211> 240
      <212> DNA
      <213> mouse

      <400> 117
ccgccaggag aggagataca cagccagtga tgtggaccac cggatggctg ttgctgctgc      60
cgcttctgct gtgtgaagga gcgcaagccc tggagtgcta cagctgcgtg cagaaggcgg     120
acgatggatg cgctccgcac aggatgaaga cagtcaaatg tggtcccggg gtggacgtct     180
gtaccgaggc cgtgggagcg gtagagacca tccacgggca attctctgtg gcggtgcggg     240

      <210> 118
      <211> 527
      <212> DNA
      <213> Human

      <400> 118
ccgtcagtct agaaggataa gagaaagaaa gttaagcaac tacaggaaat ggctttggga      60
gttccaatat cagtctatct tttattcaac gcaatgacag cactgaccga agaggcagcc     120
gtgactgtaa cacctccaat cacagcccag caaggtaact ggacagttaa caaaacagaa     180
gctcacaaca tagaaggacc catagccttg aagttctcac acctttgcct ggaagatcat     240
aacagttact gcatcaacgg tgcttgtgca ttccaccatg agctagagaa agccatctgc     300
aggtgtttta ctggttatac tggagaaagg tgtgagcact tgactttaac ttcatatgct     360
gtggattctt atgaaaaata cattgcaatt gggattggtg ttggattact attaagtggt     420
tttcttgtta ttttttactg ctatataaga aagaggtgtc taaaattgaa atcgccttac     480
aatgtctgtt ctggagaaag acgaccactg tgaggccttt gtgaaga                   527

      <210> 119
      <211> 655
      <212> DNA
      <213> Rat

      <400> 119
atggcgcgcc ccgcgccctg gtggtggctg cggccgctgg cggcgctcgc cctggcgctg      60
gcgctggtcc gggtgccctc agcccgggcc gggcagatgc cgcgccccgc agagcgcggg     120
cccccagtac ggctcttcac cgaggaggag ctggcccgct acagcggcga ggaggaggat     180
caacccatct acttggcagt gaagggagtg gtgttcgatg tcacctctgg gaaggagttt     240
tatggacgtg gagcccccta caacgccttg gccgggaagg actcgagcag aggtgtggcc     300
aagatgtcgc tggatcctgc agacctcact catgacattt ctggtctcac tgccaaggag     360
ctggaagccc tcgatgacat cttcagcaag gtgtacaaag ccaaataccc cattgttggc     420
tacacggccc gcaggatcct caacgaggat ggcagcccca acctggactt caagcctgaa     480
gaccagcccc attttgacat aaaggacgag ttctaatgtc tagctgagaa gctggttcta     540
gggagaggtg aggggacagg agttaaatgt cccacggaac aagcagggga agcctctgag     600
tgctctgcat ctgaataaaa ctgatattta actgggaaaa aaaaaaaaaa aaaaa          655

      <210> 120
      <211> 176
      <212> PRT
      <213> Rat

      <400> 120
Met Val Pro Cys Phe Leu Leu Ser Leu Leu Leu Leu Val Arg Pro Ala
 1               5                  10                  15
Pro Val Val Ala Tyr Ser Val Ser Leu Pro Ala Ser Phe Leu Glu Glu
            20                  25                  30
Val Ala Gly Ser Gly Glu Ala Glu Gly Ser Ser Ala Ser Ser Pro Ser
        35                  40                  45
```

Leu Leu Pro Pro Arg Thr Pro Ala Phe Ser Pro Thr Pro Gly Arg Thr
50 55 60
Gln Pro Thr Ala Pro Val Gly Pro Val Pro Pro Thr Asn Leu Leu Asp
65 70 75 80
Gly Ile Val Asp Phe Phe Arg Gln Tyr Val Met Leu Ile Ala Val Val
85 90 95
Gly Ser Leu Thr Phe Leu Ile Met Phe Ile Val Cys Ala Ala Leu Ile
100 105 110
Thr Arg Gln Lys His Lys Ala Thr Ala Tyr Tyr Pro Ser Ser Phe Pro
115 120 125
Glu Lys Lys Tyr Val Asp Gln Arg Asp Arg Ala Gly Gly Pro His Ala
130 135 140
Phe Ser Glu Val Pro Asp Arg Ala Pro Asp Ser Arg Gln Glu Glu Gly
145 150 155 160
Leu Asp Phe Phe Gln Gln Leu Gln Ala Asp Ile Leu Ala Cys Tyr Ser
165 170 175

<210> 121
<211> 116
<212> PRT
<213> Rat

<400> 121
Met Glu Leu Leu Tyr Trp Cys Leu Leu Cys Leu Leu Leu Pro Leu Thr
1 5 10 15
Ser Arg Thr Gln Lys Leu Pro Thr Arg Asp Glu Glu Leu Phe Gln Met
20 25 30
Gln Ile Arg Asp Lys Ala Leu Phe His Asp Ser Ser Val Ile Pro Asp
35 40 45
Gly Ala Glu Ile Ser Ser Tyr Leu Phe Arg Asp Thr Pro Arg Arg Tyr
50 55 60
Phe Phe Met Val Glu Glu Asp Asn Thr Pro Leu Ser Val Thr Val Thr
65 70 75 80
Pro Cys Asp Ala Pro Leu Glu Trp Lys Leu Ser Leu Gln Glu Leu Pro
85 90 95
Glu Glu Ser Ser Ala Asp Gly Ser Gly Asp Pro Glu Pro Leu Asp Gln
100 105 110
Gln Lys Gln Gln
115

<210> 122
<211> 64
<212> PRT
<213> Human

<400> 122
Met Asn Leu Leu Ile Gly Ser Ile Ile Leu Ser Ser Phe Leu Val Leu
1 5 10 15
Ser Asp Gly Asp Thr Thr Ala Ser Pro Ser Ser Met Ser Ser Ser Ser
20 25 30
Val Leu Asn His Ile Ser Ser Ser Ser Ser Ser Val Trp His Leu Phe
35 40 45
Asp Ile Cys Asp Ser Ser Lys Trp Asn Ala Tyr Cys Gln Val Trp Gly
50 55 60

<210> 123
<211> 68
<212> PRT
<213> Human

<400> 123

Met Leu Thr Leu Pro Ile Leu Val Cys Lys Val Gln Asp Ser Asn Arg
1 5 10 15
Arg Lys Met Leu Pro Thr Gln Phe Leu Phe Leu Leu Gly Val Leu Gly
20 25 30
Ile Phe Gly Leu Thr Phe Ala Phe Ile Ile Gly Leu Asp Gly Ser Thr
35 40 45
Gly Pro Thr Arg Phe Phe Leu Phe Gly Ile Leu Phe Ser Ile Cys Phe
50 55 60
Ser Cys Leu Leu
65

<210> 124
<211> 110
<212> PRT
<213> mouse

<400> 124
Met Ile Ser Pro Ala Trp Ser Leu Phe Leu Ile Gly Thr Lys Ile Gly
1 5 10 15
Leu Phe Phe Gln Val Ala Pro Leu Ser Val Val Ala Lys Ser Cys Pro
20 25 30
Ser Val Cys Arg Cys Asp Ala Gly Phe Ile Tyr Cys Asn Asp Arg Ser
35 40 45
Leu Thr Ser Ile Pro Val Gly Ile Pro Glu Asp Ala Thr Thr Leu Tyr
50 55 60
Leu Gln Asn Asn Gln Ile Asn Asn Val Gly Ile Pro Ser Asp Leu Lys
65 70 75 80
Asn Leu Leu Lys Val Gln Arg Ile Tyr Leu Tyr His Asn Ser Leu Asp
85 90 95
Glu Phe Pro Thr Asn Leu Pro Lys Tyr Val Lys Glu Leu His
100 105 110

<210> 125
<211> 330
<212> PRT
<213> mouse

<400> 125
Met Gly Ser Pro Arg Leu Ala Ala Leu Leu Leu Ser Leu Pro Leu Leu
1 5 10 15
Leu Ile Gly Leu Ala Val Ser Ala Arg Val Ala Cys Pro Cys Leu Arg
20 25 30
Ser Trp Thr Ser His Cys Leu Leu Ala Tyr Arg Val Asp Lys Arg Phe
35 40 45
Ala Gly Leu Gln Trp Gly Trp Phe Pro Leu Leu Val Arg Lys Ser Lys
50 55 60
Ser Pro Pro Lys Phe Glu Asp Tyr Trp Arg His Arg Thr Pro Ala Ser
65 70 75 80
Phe Gln Arg Lys Leu Leu Gly Ser Pro Ser Leu Ser Glu Glu Ser His
85 90 95
Arg Ile Ser Ile Pro Ser Ser Ala Ile Ser His Arg Gly Gln Arg Thr
100 105 110
Lys Arg Ala Gln Pro Ser Ala Ala Glu Gly Arg Glu His Leu Pro Glu
115 120 125
Ala Gly Ser Gln Lys Cys Gly Gly Pro Glu Phe Ser Phe Asp Leu Leu
130 135 140
Pro Glu Val Gln Ala Val Arg Val Thr Ile Pro Ala Gly Pro Lys Ala
145 150 155 160
Ser Val Arg Leu Cys Tyr Gln Trp Ala Leu Glu Cys Glu Asp Leu Ser
165 170 175
Ser Pro Phe Asp Thr Gln Lys Ile Val Ser Gly Gly His Thr Val Asp

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            180                 185                 190
Leu Pro Tyr Glu Phe Leu Leu Pro Cys Met Cys Ile Glu Ala Ser Tyr
        195                 200                 205
Leu Gln Glu Asp Thr Val Arg Arg Lys Lys Cys Pro Phe Gln Ser Trp
    210                 215                 220
Pro Glu Ala Tyr Gly Ser Asp Phe Trp Gln Ser Ile Arg Phe Thr Asp
225                 230                 235                 240
Tyr Ser Gln His Asn Gln Met Val Met Ala Leu Thr Leu Arg Cys Pro
                245                 250                 255
Leu Lys Leu Glu Ala Ser Leu Cys Trp Arg Gln Asp Pro Leu Thr Pro
            260                 265                 270
Cys Glu Thr Leu Pro Asn Ala Thr Ala Gln Glu Ser Glu Gly Trp Tyr
        275                 280                 285
Ile Leu Glu Asn Val Asp Leu His Pro Gln Leu Cys Phe Lys Phe Ser
    290                 295                 300
Phe Glu Asn Ser Ser His Val Glu Cys Pro His Gln Ser Gly Ser Leu
305                 310                 315                 320
Pro Ser Trp Thr Val Ser Met Asp Thr Gln
                325                 330

      <210> 126
      <211> 37
      <212> PRT
      <213> Rat

      <400> 126
Met Leu Trp Val Leu Leu Ser Leu Thr Pro Leu Leu Ser Pro Leu Ile
 1               5                  10                  15
Phe Phe Pro Val Lys Thr Val Ala Leu Glu Glu Ile Ser Thr Ile Cys
            20                  25                  30
Arg Ala Asp Val Leu
        35

      <210> 127
      <211> 42
      <212> PRT
      <213> mouse

      <400> 127
Met Gly Ser Pro Ile Ser Gly Val Cys Pro Val Leu Pro Gly Gly Leu
 1               5                  10                  15
Phe Val Ala Leu Gly Trp Ile Phe Leu Leu Phe His Arg Asp Ala Phe
            20                  25                  30
Ser Leu His Thr Met Ser Ala Gly Phe Pro
        35                  40

      <210> 128
      <211> 253
      <212> PRT
      <213> mouse

      <400> 128
Met Met Tyr Trp Ile Val Phe Ala Ile Phe Met Ala Ala Glu Thr Phe
 1               5                  10                  15
Thr Asp Ile Phe Ile Ser Trp Ser Gly Pro Arg Ile Gly Arg Pro Trp
            20                  25                  30
Gly Trp Glu Gly Pro His His His His His Leu Ala Ser Gly Ser His
        35                  40                  45
Lys Pro Leu Pro Leu Leu Thr His Arg Phe Pro Phe Tyr Tyr Glu Phe
    50                  55                  60
Lys Met Ala Phe Val Leu Trp Leu Leu Ser Pro Tyr Thr Lys Gly Ala
```

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65                  70                  75                  80
Ser Leu Leu Tyr Arg Lys Phe Val His Pro Ser Leu Ser Arg His Glu
                85                  90                  95
Lys Glu Ile Asp Ala Cys Ile Val Gln Ala Lys Glu Arg Ser Tyr Glu
            100                 105                 110
Thr Met Leu Ser Phe Gly Lys Arg Ser Leu Asn Ile Ala Ala Ser Ala
        115                 120                 125
Ala Val Gln Ala Ala Thr Lys Ser Gln Gly Ala Leu Ala Gly Arg Leu
    130                 135                 140
Arg Ser Phe Ser Met Gln Asp Leu Arg Ser Ile Pro Asp Thr Pro Val
145                 150                 155                 160
Pro Thr Tyr Gln Asp Pro Leu Tyr Leu Glu Asp Gln Val Pro Arg Arg
                165                 170                 175
Arg Pro Pro Ile Gly Tyr Arg Pro Gly Gly Leu Gln Gly Ser Asp Thr
            180                 185                 190
Glu Asp Glu Cys Trp Ser Asp Asn Glu Ile Val Pro Gln Pro Pro Val
        195                 200                 205
Arg Pro Arg Glu Lys Pro Leu Gly Arg Ser Gln Ser Leu Arg Val Val
    210                 215                 220
Lys Arg Lys Pro Leu Thr Arg Glu Gly Thr Ser Arg Ser Leu Lys Val
225                 230                 235                 240
Arg Thr Arg Lys Lys Ala Met Pro Ser Asp Met Asp Ser
                245                 250

      <210> 129
      <211> 40
      <212> PRT
      <213> mouse

      <400> 129
Met Lys Ala Met Ala Leu Ser Leu Gly Ala Ser Pro Val Leu Ala Phe
 1               5                  10                  15
Leu Leu Ser Gly Tyr Ser Asp Gly Tyr Gln Val Cys Ser Arg Phe Gly
            20                  25                  30
Ser Lys Val Pro Gln Phe Leu Asn
        35                  40

      <210> 130
      <211> 87
      <212> PRT
      <213> mouse

      <400> 130
Met Ile Ala Val Thr Phe Ala Ile Val Leu Gly Val Ile Ile Tyr Arg
 1               5                  10                  15
Ile Ser Thr Ala Ala Ala Leu Ala Met Asn Ser Ser Pro Ser Val Arg
            20                  25                  30
Ser Asn Ile Arg Val Thr Val Thr Ala Thr Ala Val Ile Ile Asn Leu
        35                  40                  45
Val Val Ile Ile Leu Leu Asp Glu Val Tyr Gly Cys Ile Ala Arg Trp
    50                  55                  60
Leu Thr Lys Ile Gly Glu Cys His Val Gln Asp Ser Ile Gly Ser Met
65                  70                  75                  80
Gly Leu Gly Gln Gly Gln Pro
                85

      <210> 131
      <211> 70
      <212> PRT
      <213> mouse
```

<400> 131

Met Phe Gly Leu Val His Val Cys Thr Cys Val Cys Val Cys Val Cys
1 5 10 15
Val Cys Val Cys Val Cys Ile Cys Ser Cys Gly Tyr Val His Val Pro
20 25 30
Cys Gly Cys Val Cys Leu Trp Gly Pro Glu Val Arg Tyr Leu Pro Leu
35 40 45
Ser Leu His Pro Gly Gly Phe Cys Phe Val Leu Phe Cys Phe Gly Pro
50 55 60
Gly Leu Ser Leu Ile Ser
65 70

<210> 132
<211> 63
<212> PRT
<213> mouse

<400> 132

Met Trp Leu Leu Val Ala Leu Thr Leu Ser Val Tyr Ser Leu Val Ala
1 5 10 15
Phe Val Thr Gly Met Leu Cys Asp Thr Val Val Ile Lys Met Leu Met
20 25 30
Ser Leu His Lys Ser Ser Lys Leu Asn Pro Arg Ala Lys Cys Gly Gly
35 40 45
Val Pro Leu Ile Pro Ala Leu Trp Gly Gln Val Gln Val Val Leu
50 55 60

<210> 133
<211> 39
<212> PRT
<213> mouse

<400> 133

Met Asp Asn Thr Leu Ser Ile Ile Ile Tyr Leu Leu Phe Ile Phe Ala
1 5 10 15
Ile Ser Val Leu Asp Ser Gln Leu Ser Thr Arg Cys Leu Trp Trp Phe
20 25 30
Ser Lys Asp Leu Glu Val Thr
35

<210> 134
<211> 90
<212> PRT
<213> Rat

<400> 134

Met Pro Thr Met Trp Pro Leu Leu His Val Leu Trp Leu Ala Leu Val
1 5 10 15
Cys Gly Ser Val His Thr Thr Leu Ser Lys Ser Asp Ala Lys Lys Ala
20 25 30
Ala Ser Lys Thr Leu Leu Glu Lys Thr Gln Phe Ser Asp Lys Pro Val
35 40 45
Gln Asp Arg Gly Leu Val Val Thr Asp Ile Lys Ala Glu Asp Val Val
50 55 60
Leu Glu His Arg Ser Tyr Cys Ser Ala Arg Ala Arg Glu Arg Asn Phe
65 70 75 80
Ala Gly Glu Val Leu Gly Ile Cys His Ser
85 90

<210> 135
<211> 193

<212> PRT
<213> Rat

<400> 135
Met Thr Ser Gly Pro Gly Gly Pro Ala Ala Ala Thr Gly Gly Gly Lys
1 5 10 15
Asp Thr His Gln Trp Tyr Val Cys Asn Arg Glu Lys Leu Cys Glu Ser
20 25 30
Leu Gln Ser Val Phe Val Gln Ser Tyr Leu Asp Gln Gly Thr Gln Ile
35 40 45
Phe Leu Asn Asn Ser Ile Glu Lys Ser Gly Trp Leu Phe Ile Gln Leu
50 55 60
Tyr His Ser Phe Val Ser Ser Val Phe Thr Leu Phe Met Ser Arg Thr
65 70 75 80
Ser Ile Asn Gly Leu Leu Gly Arg Gly Ser Met Phe Val Phe Ser Pro
85 90 95
Asp Gln Phe Gln Arg Leu Leu Lys Ile Asn Pro Asp Trp Lys Thr His
100 105 110
Arg Leu Leu Asp Leu Gly Ala Gly Asp Gly Glu Val Thr Lys Ile Met
115 120 125
Ser Pro His Phe Glu Glu Ile Tyr Ala Thr Glu Leu Ser Glu Thr Met
130 135 140
Ile Trp Gln Leu Gln Lys Lys Lys Tyr Arg Val Leu Gly Ile Asn Glu
145 150 155 160
Trp Gln Asn Thr Gly Phe Gln Tyr Asp Val Ile Ser Cys Leu Asn Leu
165 170 175
Leu Asp Arg Cys Asp Gln Pro Leu Thr Leu Leu Lys Asp Ile Arg Met
180 185 190
Ser

<210> 136
<211> 106
<212> PRT
<213> Rat

<400> 136
Met Ala Ala Pro Met Asp Arg Thr His Gly Gly Arg Ala Ala Arg Ala
1 5 10 15
Leu Arg Arg Ala Leu Ala Leu Ala Ser Leu Ala Gly Leu Leu Leu Ser
20 25 30
Gly Leu Ala Gly Ala Leu Pro Thr Leu Gly Pro Gly Trp Arg Arg Gln
35 40 45
Asn Pro Glu Pro Pro Ala Ser Arg Thr Arg Ser Leu Leu Leu Asp Ala
50 55 60
Ala Ser Gly Gln Leu Arg Leu Glu Tyr Gly Phe His Pro Asp Ala Val
65 70 75 80
Ala Trp Ala Asn Leu Thr Asn Ala Ile Arg Glu Thr Gly Trp Ala Tyr
85 90 95
Leu Asp Leu Gly Thr Asn Gly Ser Tyr Lys
100 105

<210> 137
<211> 286
<212> PRT
<213> Rat

<400> 137
Met Ala Ala Ala Met Pro Leu Gly Leu Ser Leu Leu Leu Leu Val Leu
1 5 10 15
Val Gly Gln Gly Cys Cys Gly Arg Val Glu Gly Pro Arg Asp Ser Leu

20 25 30
Arg Glu Glu Leu Val Ile Thr Pro Leu Pro Ser Gly Asp Val Ala Ala
35 40 45
Thr Phe Gln Phe Arg Thr Arg Trp Asp Ser Asp Leu Gln Arg Glu Gly
50 55 60
Val Ser His Tyr Arg Leu Phe Pro Lys Ala Leu Gly Gln Leu Ile Ser
65 70 75 80
Lys Tyr Ser Leu Arg Glu Leu His Leu Ser Phe Thr Gln Gly Phe Trp
85 90 95
Arg Thr Arg Tyr Trp Gly Pro Pro Phe Leu Gln Ala Pro Ser Gly Ala
100 105 110
Glu Leu Trp Val Trp Phe Gln Asp Thr Val Thr Asp Val Asp Lys Ser
115 120 125
Trp Lys Glu Leu Ser Asn Val Leu Ser Gly Ile Phe Cys Ala Ser Leu
130 135 140
Asn Phe Ile Asp Ser Thr Asn Thr Val Thr Pro Thr Ala Ser Phe Lys
145 150 155 160
Pro Leu Gly Leu Ala Asn Asp Thr Asp His Tyr Phe Leu Arg Tyr Ala
165 170 175
Val Leu Pro Arg Glu Val Val Cys Thr Glu Asn Leu Thr Pro Trp Lys
180 185 190
Lys Leu Leu Pro Cys Ser Ser Lys Ala Gly Leu Ser Val Leu Leu Lys
195 200 205
Ala Asp Arg Leu Phe His Thr Ser Tyr His Ser Gln Ala Val His Ile
210 215 220
Arg Pro Ile Cys Arg Asn Ala His Cys Thr Ser Ile Ser Trp Glu Leu
225 230 235 240
Arg Gln Thr Leu Ser Val Val Phe Asp Ala Phe Ile Thr Gly Gln Gly
245 250 255
Lys Lys Glu Ala Cys Pro Leu Ala Ser Gln Ser Leu Val Tyr Val Asp
260 265 270
Ile Thr Gly Tyr Ser Gln Asp Asn Glu Thr Leu Glu Val Ser
275 280 285

<210> 138
<211> 198
<212> PRT
<213> Rat

<400> 138
Met Thr Val Phe Arg Lys Val Thr Thr Met Ile Ser Trp Met Leu Leu
1 5 10 15
Ala Cys Ala Leu Pro Cys Ala Ala Asp Pro Met Leu Gly Ala Phe Ala
20 25 30
Arg Arg Asp Phe Gln Lys Gly Gly Pro Gln Leu Val Cys Ser Leu Pro
35 40 45
Gly Pro Gln Gly Pro Pro Gly Pro Pro Gly Ala Pro Gly Ser Ser Gly
50 55 60
Met Val Gly Arg Met Gly Phe Pro Gly Lys Asp Gly Gln Asp Gly Gln
65 70 75 80
Asp Gly Asp Arg Gly Asp Ser Gly Glu Glu Gly Pro Pro Gly Arg Thr
85 90 95
Gly Asn Arg Gly Lys Gln Gly Pro Lys Gly Lys Ala Gly Ala Ile Gly
100 105 110
Arg Ala Gly Pro Arg Gly Pro Lys Gly Val Ser Gly Thr Pro Gly Lys
115 120 125
His Gly Ile Pro Gly Lys Lys Gly Pro Lys Gly Lys Lys Gly Glu Pro
130 135 140
Gly Leu Pro Gly Pro Cys Ser Cys Gly Ser Ser Arg Ala Lys Ser Ala
145 150 155 160
Phe Ser Val Ala Val Thr Lys Ser Tyr Pro Arg Glu Arg Leu Pro Ile

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                165                 170                 175
Lys Phe Asp Lys Ile Leu Met Asn Glu Gly Gly His Tyr Asn Ala Ser
            180                 185                 190
Ser Gly Lys Phe Val Cys
        195
```

<210> 139
<211> 233
<212> PRT
<213> Rat

<400> 139

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Met Ala Ser Ala Leu Glu Glu Leu Gln Lys Asp Leu Glu Glu Val Lys
 1               5                  10                  15
Val Leu Leu Glu Lys Ser Thr Arg Lys Arg Leu Arg Asp Thr Leu Thr
            20                  25                  30
Asn Glu Lys Ser Lys Ile Glu Thr Glu Leu Arg Asn Lys Met Gln Gln
        35                  40                  45
Lys Ser Gln Lys Lys Pro Glu Phe Asp Asn Glu Lys Pro Ala Ala Val
    50                  55                  60
Val Ala Pro Leu Thr Thr Gly Tyr Thr Val Lys Ile Ser Asn Tyr Gly
65                  70                  75                  80
Trp Asp Gln Ser Asp Lys Phe Val Lys Ile Tyr Ile Thr Leu Thr Gly
                85                  90                  95
Val His Gln Val Pro Ala Glu Asn Val Gln Val His Phe Thr Glu Arg
            100                 105                 110
Ser Phe Asp Leu Leu Val Lys Asn Leu Asn Gly Lys Asn Tyr Ser Met
        115                 120                 125
Ile Val Asn Asn Leu Leu Lys Pro Ile Ser Val Glu Ser Ser Ser Lys
    130                 135                 140
Lys Val Lys Thr Asp Thr Val Ile Ile Leu Cys Arg Lys Lys Ala Glu
145                 150                 155                 160
Asn Thr Arg Trp Asp Tyr Leu Thr Gln Val Glu Lys Glu Cys Lys Glu
                165                 170                 175
Lys Glu Lys Pro Ser Tyr Asp Thr Glu Ala Asp Pro Ser Glu Gly Leu
            180                 185                 190
Met Asn Val Leu Lys Lys Ile Tyr Glu Asp Gly Asp Asp Asp Met Lys
        195                 200                 205
Arg Thr Ile Asn Lys Ala Trp Val Glu Ser Arg Glu Lys Gln Ala Arg
    210                 215                 220
Glu Asp Thr Glu Phe Leu Gln Pro Gly
225                 230
```

<210> 140
<211> 38
<212> PRT
<213> Human

<400> 140

```
Met Gly Leu Ala Leu Cys Leu Ala Ser Ala Gly Ile Ser Gly Ser Arg
 1               5                  10                  15
Ser Ala Phe Leu Gly Val Pro Arg Pro Arg Pro Thr Leu Ile Lys Leu
            20                  25                  30
Ile Asp Thr Val Asp Leu
        35
```

<210> 141
<211> 322
<212> PRT
<213> mouse

<400> 141

```
Met Asp Ala Arg Trp Trp Ala Val Val Val Leu Ala Thr Leu Pro Ser
 1               5                  10                  15
Leu Gly Ala Gly Gly Glu Ser Pro Glu Ala Pro Pro Gln Ser Trp Thr
            20                  25                  30
Gln Leu Trp Leu Phe Arg Phe Leu Leu Asn Val Ala Gly Tyr Ala Ser
        35                  40                  45
Phe Met Val Pro Gly Tyr Leu Leu Val Gln Tyr Leu Arg Arg Lys Asn
    50                  55                  60
Tyr Leu Glu Thr Gly Arg Gly Leu Cys Phe Pro Leu Val Lys Ala Cys
65                  70                  75                  80
Val Phe Gly Asn Glu Pro Lys Ala Pro Asp Glu Val Leu Leu Ala Pro
                85                  90                  95
Arg Thr Glu Thr Ala Glu Ser Thr Pro Ser Trp Gln Val Leu Lys Leu
            100                 105                 110
Val Phe Cys Ala Ser Gly Leu Gln Val Ser Tyr Leu Thr Trp Gly Ile
        115                 120                 125
Leu Gln Glu Arg Val Met Thr Gly Ser Tyr Gly Ala Thr Ala Thr Ser
    130                 135                 140
Pro Gly Glu His Phe Thr Asp Ser Gln Phe Leu Val Leu Met Asn Arg
145                 150                 155                 160
Val Leu Ala Leu Val Val Ala Gly Leu Tyr Cys Val Leu Arg Lys Gln
                165                 170                 175
Pro Arg His Gly Ala Pro Met Tyr Arg Tyr Ser Phe Ala Ser Leu Ser
            180                 185                 190
Asn Val Leu Ser Ser Trp Cys Gln Tyr Glu Ala Leu Lys Phe Val Ser
        195                 200                 205
Phe Pro Thr Gln Val Leu Ala Lys Ala Ser Lys Val Ile Pro Val Met
    210                 215                 220
Met Met Gly Lys Leu Val Ser Arg Arg Ser Tyr Glu His Trp Glu Tyr
225                 230                 235                 240
Leu Thr Ala Gly Leu Ile Ser Ile Gly Val Ser Met Phe Leu Leu Ser
                245                 250                 255
Ser Gly Pro Glu Pro Arg Ser Ser Pro Ala Thr Thr Leu Ser Gly Leu
            260                 265                 270
Val Leu Leu Ala Gly Tyr Ile Ala Phe Asp Ser Phe Thr Ser Asn Trp
        275                 280                 285
Gln Asp Ala Leu Phe Ala Tyr Lys Met Ser Ser Val Gln Met Met Phe
    290                 295                 300
Gly Val Asn Leu Phe Ser Cys Leu Phe Thr Val Gly Ser Leu Leu Glu
305                 310                 315                 320
Gln Gly
```

<210> 142
<211> 312
<212> PRT
<213> mouse

<400> 142

```
Met Leu Cys Leu Cys Leu Tyr Val Pro Ile Ala Gly Ala Ala Gln Thr
 1               5                  10                  15
Glu Phe Gln Tyr Phe Glu Ser Lys Gly Leu Pro Ala Glu Leu Lys Ser
            20                  25                  30
Ile Phe Lys Leu Ser Val Phe Ile Pro Ser Gln Glu Phe Ser Thr Tyr
        35                  40                  45
Arg Gln Trp Lys Gln Lys Ile Val Gln Ala Gly Asp Lys Asp Leu Asp
    50                  55                  60
Gly Gln Leu Asp Phe Glu Glu Phe Val His Tyr Leu Gln Asp His Glu
65                  70                  75                  80
Lys Lys Leu Arg Leu Val Phe Lys Ser Leu Asp Lys Lys Asn Asp Gly
```

```
                85                      90                      95
Arg Ile Asp Ala Gln Glu Ile Met Gln Ser Leu Arg Asp Leu Gly Val
            100                     105                     110
Lys Ile Ser Glu Gln Gln Ala Glu Lys Ile Leu Lys Ser Met Asp Lys
        115                     120                     125
Asn Gly Thr Met Thr Ile Asp Trp Asn Glu Trp Arg Asp Tyr His Leu
    130                     135                     140
Leu His Pro Val Glu Asn Ile Pro Glu Ile Ile Leu Tyr Trp Lys His
145                     150                     155                     160
Ser Thr Ile Phe Asp Val Gly Glu Asn Leu Thr Val Pro Asp Glu Phe
                165                     170                     175
Thr Val Glu Glu Arg Gln Thr Gly Met Trp Trp Arg His Leu Val Ala
            180                     185                     190
Gly Gly Gly Ala Gly Ala Val Ser Arg Thr Cys Thr Ala Pro Leu Asp
        195                     200                     205
Arg Leu Lys Val Leu Met Gln Val His Ala Ser Arg Ser Asn Asn Met
    210                     215                     220
Cys Ile Val Gly Gly Phe Thr Gln Met Ile Arg Glu Gly Gly Ala Lys
225                     230                     235                     240
Ser Leu Trp Arg Gly Asn Gly Ile Asn Val Leu Lys Ile Ala Pro Glu
                245                     250                     255
Ser Ala Ile Lys Phe Met Ala Tyr Glu Gln Met Lys Arg Leu Val Gly
            260                     265                     270
Ser Asp Gln Glu Thr Leu Arg Ile His Glu Arg Leu Val Ala Gly Ser
        275                     280                     285
Leu Ala Gly Ala Ile Ala Gln Ser Ser Ile Tyr Pro Met Glu Val Leu
    290                     295                     300
Lys Thr Arg Met Ala Leu Arg Lys
305                     310

<210> 143
<211> 163
<212> PRT
<213> Rat

<400> 143
Met Pro Leu Val Thr Thr Leu Phe Tyr Ala Cys Phe Tyr His Tyr Thr
 1               5                  10                  15
Glu Ser Glu Gly Thr Phe Ser Ser Pro Val Asn Leu Lys Lys Thr Phe
            20                  25                  30
Lys Ile Pro Asp Arg Gln Tyr Val Leu Thr Ala Leu Ala Ala Arg Ala
        35                  40                  45
Lys Leu Arg Ala Trp Asn Asp Val Asp Ala Leu Phe Thr Thr Lys Asn
    50                  55                  60
Trp Leu Gly Tyr Thr Lys Lys Arg Ala Pro Ile Gly Phe His Arg Val
65                  70                  75                  80
Val Glu Ile Leu His Lys Asn Ser Ala Pro Val Gln Ile Leu Gln Glu
                85                  90                  95
Tyr Val Asn Leu Val Glu Asp Val Asp Thr Lys Leu Asn Leu Ala Thr
            100                 105                 110
Lys Phe Lys Cys His Asp Val Val Ile Asp Thr Cys Arg Asp Leu Lys
        115                 120                 125
Asp Arg Gln Gln Leu Leu Ala Tyr Arg Ser Lys Val Asp Lys Gly Ser
    130                 135                 140
Ala Glu Glu Glu Lys Ile Asp Val Ile Leu Ser Ser Ser Gln Ile Arg
145                 150                 155                 160
Trp Lys Asn

<210> 144
<211> 330
```

<212> PRT
<213> Rat

<400> 144
Met Ala Gly Trp Ala Gly Ala Glu Leu Ser Val Leu Asn Pro Leu Arg
1 5 10 15
Ala Leu Trp Leu Leu Leu Ala Ala Ala Phe Leu Leu Ala Leu Leu Leu
20 25 30
Gln Leu Ala Pro Ala Arg Leu Leu Pro Ser Cys Ala Leu Phe Gln Asp
35 40 45
Leu Ile Arg Tyr Gly Lys Thr Lys Gln Ser Gly Ser Arg Arg Pro Ala
50 55 60
Val Cys Arg Ala Phe Asp Val Pro Lys Arg Tyr Phe Ser His Phe Tyr
65 70 75 80
Val Val Ser Val Leu Trp Asn Gly Ser Leu Leu Trp Phe Leu Ser Gln
85 90 95
Ser Leu Phe Leu Gly Ala Pro Phe Pro Ser Trp Leu Trp Ala Leu Leu
100 105 110
Arg Thr Leu Gly Val Thr Gln Phe Gln Ala Leu Gly Met Glu Ser Lys
115 120 125
Ala Ser Arg Ile Gln Ala Gly Glu Leu Ala Leu Ser Thr Phe Leu Val
130 135 140
Leu Val Phe Leu Trp Val His Ser Leu Arg Arg Leu Phe Glu Cys Phe
145 150 155 160
Tyr Val Ser Val Phe Ser Asn Thr Ala Ile His Val Val Gln Tyr Cys
165 170 175
Phe Gly Leu Val Tyr Tyr Val Leu Val Gly Leu Thr Val Leu Ser Gln
180 185 190
Val Pro Met Asn Asp Lys Asn Val Tyr Ala Leu Gly Lys Asn Leu Leu
195 200 205
Leu Gln Ala Arg Trp Phe His Ile Leu Gly Met Met Met Phe Phe Trp
210 215 220
Ser Ser Ala His Gln Tyr Lys Cys His Val Ile Leu Ser Asn Leu Arg
225 230 235 240
Arg Asn Lys Lys Gly Val Val Ile His Cys Gln His Arg Ile Pro Phe
245 250 255
Gly Asp Trp Phe Glu Tyr Val Ser Ser Ala Asn Tyr Leu Ala Glu Leu
260 265 270
Met Ile Tyr Ile Ser Met Ala Val Thr Phe Gly Leu His Asn Val Thr
275 280 285
Trp Trp Leu Val Val Thr Tyr Val Phe Phe Ser Gln Ala Leu Ser Ala
290 295 300
Phe Phe Asn His Arg Phe Tyr Lys Ser Thr Phe Val Ser Tyr Pro Lys
305 310 315 320
His Arg Lys Ala Phe Leu Pro Phe Leu Phe
325 330

<210> 145
<211> 301
<212> PRT
<213> Rat

<400> 145
Met Leu Val Ala Phe Leu Gly Ala Ser Ala Val Thr Ala Ser Thr Gly
1 5 10 15
Leu Leu Trp Lys Lys Ala His Ala Glu Ser Pro Pro Ser Val Asn Ser
20 25 30
Lys Lys Thr Asp Ala Gly Asp Lys Gly Lys Ser Lys Asp Thr Arg Glu
35 40 45
Val Ser Ser His Glu Gly Ser Ala Ala Asp Thr Ala Ala Glu Pro Tyr
50 55 60

Pro Glu Glu Lys Lys Lys Lys Arg Ser Gly Phe Arg Asp Arg Lys Val
65 70 75 80
Met Glu Tyr Glu Asn Arg Ile Arg Ala Tyr Ser Thr Pro Asp Lys Ile
85 90 95
Phe Arg Tyr Phe Ala Thr Leu Lys Val Ile Asn Glu Pro Gly Glu Thr
100 105 110
Glu Val Phe Met Thr Pro Gln Asp Phe Val Arg Ser Ile Thr Pro Asn
115 120 125
Glu Lys Gln Pro Glu His Leu Gly Leu Asp Gln Tyr Ile Ile Lys Arg
130 135 140
Phe Asp Gly Lys Lys Ile Ala Gln Glu Arg Glu Lys Phe Ala Asp Glu
145 150 155 160
Gly Ser Ile Phe Tyr Thr Leu Gly Glu Cys Gly Leu Ile Ser Phe Ser
165 170 175
Asp Tyr Ile Phe Leu Thr Thr Val Leu Ser Thr Pro Gln Arg Asn Phe
180 185 190
Glu Ile Ala Phe Lys Met Phe Asp Leu Asn Gly Asp Gly Glu Val Asp
195 200 205
Met Glu Glu Phe Glu Gln Val Gln Ser Ile Ile Arg Ser Gln Thr Ser
210 215 220
Met Gly Met Arg His Arg Asp Arg Pro Thr Thr Gly Asn Thr Leu Lys
225 230 235 240
Ser Gly Leu Cys Ser Ala Leu Thr Thr Tyr Phe Phe Gly Ala Asp Leu
245 250 255
Lys Gly Lys Leu Thr Ile Lys Asn Phe Leu Glu Phe Gln Arg Lys Leu
260 265 270
Gln Arg Cys Leu Leu Gly Leu Pro Val Trp Glu Gly Ser Pro His Leu
275 280 285
Pro Thr Gly His Trp Leu Arg Glu Leu Trp Ser Leu Leu
290 295 300

<210> 146
<211> 61
<212> PRT
<213> Rat

<400> 146
Met Glu Asn Ile Tyr Tyr Thr Asn Leu Ile Thr Ile Leu Gly Asn Lys
1 5 10 15
His Ala Asn Gln Met Glu Leu Asn Leu Gln Ala Leu Ile Leu Ser Pro
20 25 30
Trp Phe Ala Val Cys Ala Pro Pro Gly Phe Ala Arg Asp Gln Ala Val
35 40 45
Arg Gly Leu Ala Leu Ala Gly Arg Arg Ile Thr Val Val
50 55 60

<210> 147
<211> 105
<212> PRT
<213> Rat

<400> 147
Met Leu Arg Arg Gln Leu Val Trp Trp His Leu Leu Ala Leu Leu Phe
1 5 10 15
Leu Pro Phe Cys Leu Cys Gln Asp Glu Tyr Met Glu Ser Pro Gln Ala
20 25 30
Gly Gly Leu Pro Pro Asp Cys Ser Lys Cys Cys His Gly Asp Tyr Gly
35 40 45
Phe Arg Gly Tyr Gln Gly Pro Pro Gly Pro Pro Gly Pro Pro Gly Ile
50 55 60
Pro Gly Asn His Gly Asn Asn Gly Asn Asn Gly Ala Thr Gly His Glu

```
65                  70                  75                  80
Gly Ala Lys Gly Glu Lys Gly Asp Lys Gly Asp Leu Gly Pro Arg Gly
                85                  90                  95
Glu Arg Gly Gln His Gly Pro Lys Gly
            100                 105

      <210> 148
      <211> 210
      <212> PRT
      <213> Rat

      <400> 148
Met Leu Gly Ala Thr Ser Leu Ser Trp Pro Trp Val Leu Trp Ala Val
 1               5                  10                  15
Ala Gln Arg Asp Ser Val Asp Ala Ile Gly Met Phe Leu Gly Gly Leu
            20                  25                  30
Val Ala Thr Ile Phe Leu Asp Ile Ile Tyr Ile Ser Ile Phe Tyr Ser
        35                  40                  45
Ser Val Ala Val Gly Asp Thr Gly Arg Phe Ser Ala Gly Met Ala Ile
    50                  55                  60
Phe Ser Leu Leu Leu Gln Ala Leu Leu Leu Leu Pro Arg Leu Pro His
65                  70                  75                  80
Ala Pro Gly Ser Glu Gly Val Ser Ser Arg Ser Ala Arg Ile Ser Ser
                85                  90                  95
Asp Leu Leu Arg Asn Ile Val Pro Thr Arg Gln Leu Thr Arg Gln Thr
            100                 105                 110
His Leu Gln Thr Pro Leu Gln Ala Trp Arg Thr Arg Ala Lys Leu Pro
        115                 120                 125
Pro Gly Gly Thr Glu Ala Val Pro Gly Arg Pro Gly Ala Gln Gln Asp
    130                 135                 140
Ala Cys His Leu Leu Tyr Trp Thr Tyr Asn Gly Val Ser Ser Ile Pro
145                 150                 155                 160
Cys His Arg Gly Gly Leu Ser His Val Pro Ser Glu Val Pro Ala Glu
                165                 170                 175
Lys Ser Pro Val Leu Ile Leu His Ala Ala Pro Pro Phe Lys Thr Pro
            180                 185                 190
Val Asn Pro Trp Ala Arg Thr Val Val Gly Phe Phe Pro Ser Ser Pro
        195                 200                 205
Ser Leu
    210

      <210> 149
      <211> 301
      <212> PRT
      <213> Rat

      <400> 149
Met Leu Val Ala Phe Leu Gly Ala Ser Ala Val Thr Ala Ser Thr Gly
 1               5                  10                  15
Leu Leu Trp Lys Lys Ala His Ala Glu Ser Pro Pro Ser Val Asn Ser
            20                  25                  30
Lys Lys Thr Asp Ala Gly Asp Lys Gly Lys Ser Lys Asp Thr Arg Glu
        35                  40                  45
Val Ser Ser His Glu Gly Ser Ala Ala Asp Thr Ala Ala Glu Pro Tyr
    50                  55                  60
Pro Glu Glu Lys Lys Lys Lys Arg Ser Gly Phe Arg Asp Arg Lys Val
65                  70                  75                  80
Met Glu Tyr Glu Asn Arg Ile Arg Ala Tyr Ser Thr Pro Asp Lys Ile
                85                  90                  95
Phe Arg Tyr Phe Ala Thr Leu Lys Val Ile Asn Glu Pro Gly Glu Thr
            100                 105                 110
```

Glu Val Phe Met Thr Pro Gln Asp Phe Val Arg Ser Ile Thr Pro Asn
        115   120   125
Glu Lys Gln Pro Glu His Leu Gly Leu Asp Gln Tyr Ile Ile Lys Arg
    130   135   140
Phe Asp Gly Lys Lys Ile Ala Gln Glu Arg Glu Lys Phe Ala Asp Glu
145   150   155   160
Gly Ser Ile Phe Tyr Thr Leu Gly Glu Cys Gly Leu Ile Ser Phe Ser
                165   170   175
Asp Tyr Ile Phe Leu Thr Thr Val Leu Ser Thr Pro Gln Arg Asn Phe
            180   185   190
Glu Ile Ala Phe Lys Met Phe Asp Leu Asn Gly Asp Gly Glu Val Asp
        195   200   205
Met Glu Glu Phe Glu Gln Val Gln Ser Ile Ile Arg Ser Gln Thr Ser
    210   215   220
Met Gly Met Arg His Arg Asp Arg Pro Thr Thr Gly Asn Thr Leu Lys
225   230   235   240
Ser Gly Leu Cys Ser Ala Leu Thr Thr Tyr Phe Phe Gly Ala Asp Leu
                245   250   255
Lys Gly Lys Leu Thr Ile Lys Asn Phe Leu Glu Phe Gln Arg Lys Leu
            260   265   270
Gln Arg Cys Leu Leu Gly Leu Pro Val Trp Glu Gly Ser Pro His Leu
        275   280   285
Pro Thr Gly His Trp Leu Arg Glu Leu Trp Ser Leu Leu
    290   295   300

<210> 150
<211> 80
<212> PRT
<213> Human

<400> 150
Met Lys Leu Ser Gly Met Phe Leu Leu Leu Ser Leu Ala Leu Phe Cys
1   5   10   15
Phe Leu Thr Gly Val Phe Ser Gln Gly Gly Gln Val Asp Cys Gly Glu
            20   25   30
Phe Gln Asp Thr Lys Val Tyr Cys Thr Arg Glu Ser Asn Pro His Cys
        35   40   45
Gly Ser Asp Gly Gln Thr Tyr Gly Asn Lys Cys Ala Phe Cys Lys Ala
    50   55   60
Ile Val Lys Ser Gly Gly Lys Ile Ser Leu Lys His Pro Gly Lys Cys
65   70   75   80

<210> 151
<211> 27
<212> PRT
<213> mouse

<400> 151
Met Leu Lys Ala Ser Leu His Ile Leu Phe Leu Gly Ile Leu Asn Val
1   5   10   15
Pro Ile Val Asp Thr Ser Thr Lys Thr Gly Val
            20   25

<210> 152
<211> 86
<212> PRT
<213> mouse

<400> 152
Met Leu Gln Gly Pro Ala Pro Ser Cys Phe Trp Val Phe Ser Gly Ile
1   5   10   15

```
Cys Val Phe Trp Asp Phe Ile Phe Ile Ile Phe Phe Asn Val Leu Ser
            20                  25                  30
Leu Gly Asn Arg Glu Ile Ser Ala Lys Asp Phe Ala Asp Gln Pro Ala
        35                  40                  45
Gly Ala Gln Gly Met Trp Gly Ile Trp Gly His Thr Ile Thr Cys Gly
    50                  55                  60
Leu Ala Pro Gly Ala Lys Pro Cys Ser Leu Lys Arg Glu Gly Pro Asp
65                  70                  75                  80
Leu Leu Ser Phe Pro Pro
                85

      <210> 153
      <211> 72
      <212> PRT
      <213> mouse

      <400> 153
Met Ser Ala Ile Phe Asn Phe Gln Ser Leu Leu Thr Val Ile Leu Leu
 1               5                  10                  15
Leu Ile Cys Thr Cys Ala Tyr Ile Arg Ser Leu Ala Pro Ser Ile Leu
            20                  25                  30
Asp Arg Asn Lys Thr Gly Leu Leu Gly Ile Phe Trp Lys Cys Ala Arg
        35                  40                  45
Ile Gly Glu Arg Lys Ser Pro Tyr Val Ala Ile Cys Cys Ile Val Met
    50                  55                  60
Ala Phe Ser Ile Leu Phe Ile Gln
65                  70

      <210> 154
      <211> 169
      <212> PRT
      <213> mouse

      <400> 154
Met Ser Gly Leu Arg Thr Leu Leu Gly Leu Gly Leu Leu Val Ala Gly
 1               5                  10                  15
Ser Arg Leu Pro Arg Val Ile Ser Gln Gln Ser Val Cys Arg Ala Arg
            20                  25                  30
Pro Ile Trp Trp Gly Thr Gln Arg Arg Gly Ser Glu Thr Met Ala Gly
        35                  40                  45
Ala Ala Val Lys Tyr Leu Ser Gln Glu Glu Ala Gln Ala Val Asp Gln
    50                  55                  60
Glu Leu Phe Asn Glu Tyr Gln Phe Ser Val Asp Gln Leu Met Glu Leu
65                  70                  75                  80
Ala Gly Leu Ser Cys Ala Thr Ala Ile Ala Lys Ala Tyr Pro Pro Thr
                85                  90                  95
Ser Met Ser Lys Ser Pro Pro Thr Val Leu Val Ile Cys Gly Pro Gly
            100                 105                 110
Asn Asn Gly Gly Asp Gly Leu Val Cys Ala Arg His Leu Lys Leu Phe
        115                 120                 125
Gly Tyr Gln Pro Thr Ile Tyr Tyr Pro Lys Arg Pro Asn Lys Pro Leu
    130                 135                 140
Phe Thr Gly Leu Val Thr Gln Cys Gln Lys Met Asp Ile Pro Phe Leu
145                 150                 155                 160
Gly Glu Met Pro Pro Glu Asp Gly Met
                165

      <210> 155
      <211> 61
      <212> PRT
      <213> mouse
```

<400> 155
Met Glu Lys Gln Met Asp Ala Ser Val Ser Val Ile Phe Gly Ser Ile
1   5   10   15
Val Ile Ser Ala Phe Leu Tyr Leu Ser Leu Ala Gly Pro Trp Ala Val
            20   25   30
Thr Val Thr Gln Met Arg Thr Ile Ile Ile Thr Met Asp Gln Leu Arg
        35   40   45
Asp Ala Leu Ile Leu Asp Gln Leu Lys Val Ala Val Ser
    50   55   60

<210> 156
<211> 131
<212> PRT
<213> mouse

<400> 156
Met Ala Pro Ser Leu Trp Lys Gly Leu Val Gly Val Gly Leu Phe Ala
1   5   10   15
Leu Ala His Ala Ala Phe Ser Ala Ala Gln His Arg Ser Tyr Met Arg
            20   25   30
Leu Thr Glu Lys Glu Asp Glu Ser Leu Pro Ile Asp Ile Val Leu Gln
        35   40   45
Thr Leu Leu Ala Phe Ala Val Thr Cys Tyr Gly Ile Val His Ile Ala
    50   55   60
Gly Glu Phe Lys Asp Met Asp Ala Thr Ser Glu Leu Lys Asn Lys Thr
65   70   75   80
Phe Asp Thr Leu Arg Asn His Pro Ser Phe Tyr Val Phe Asn His Arg
                85   90   95
Gly Arg Val Leu Phe Arg Pro Ser Asp Ala Thr Asn Ser Ser Asn Leu
            100   105   110
Asp Ala Leu Ser Ser Asn Thr Ser Leu Lys Leu Arg Lys Phe Asp Ser
        115   120   125
Leu Arg Arg
    130

<210> 157
<211> 133
<212> PRT
<213> mouse

<400> 157
Met Arg Leu Leu Ala Ala Ala Leu Leu Leu Leu Leu Leu Ala Leu Cys
1   5   10   15
Ala Ser Arg Val Asp Gly Ser Lys Cys Lys Cys Ser Arg Lys Gly Pro
            20   25   30
Lys Ile Arg Tyr Ser Asp Val Lys Lys Leu Glu Met Lys Pro Lys Tyr
        35   40   45
Pro His Cys Glu Glu Lys Met Val Ile Val Thr Thr Lys Glu His Val
    50   55   60
Gln Gly Thr Gly Ala Arg Ser Thr Ala Cys Thr Leu Ser Cys Arg Ala
65   70   75   80
Pro Asn Ala Ser Ser Ser Gly Thr Met Pro Gly Thr Arg Ser Ala Gly
                85   90   95
Ser Thr Lys Asn Arg Val Asp Asp His Gly Lys Lys Asn Ser Arg Pro
            100   105   110
Val Glu Arg Leu Gln Gln Arg Thr Leu Gln Ile Lys Ile Lys Ala Leu
        115   120   125
Ser Phe Ser Gln Ala
    130

<210> 158
<211> 78
<212> PRT
<213> mouse

<400> 158
Gly Thr Arg Lys Pro Leu Pro Met Glu Ala His Ser Arg Arg Glu Lys
1 5 10 15
Ala Ser Gly Leu Arg Leu Ala Trp His Tyr Glu Cys Ser Gly Val Ser
20 25 30
Val Trp Trp Met Cys Val Leu Gly Trp Leu Ser Phe Leu Val Phe Leu
35 40 45
Leu Phe Ser Leu Val Cys Ser Phe Pro Ser Pro Ile Asn His Ser His
50 55 60
Met Leu Pro Cys Leu Phe Leu Arg Gly Gly Gly Ser Asn Val
65 70 75

<210> 159
<211> 206
<212> PRT
<213> mouse

<400> 159
Met Leu Pro Pro Ala Ile His Leu Ser Leu Ile Pro Leu Leu Cys Ile
1 5 10 15
Leu Met Arg Asn Cys Leu Ala Phe Lys Asn Asp Ala Thr Glu Ile Leu
20 25 30
Tyr Ser His Val Val Lys Pro Val Pro Ala His Pro Ser Ser Asn Ser
35 40 45
Thr Leu Asn Gln Ala Arg Asn Gly Gly Arg His Phe Ser Ser Thr Gly
50 55 60
Leu Asp Arg Asn Ser Arg Val Gln Val Gly Cys Arg Glu Leu Arg Ser
65 70 75 80
Thr Lys Tyr Ile Ser Asp Gly Gln Cys Thr Ser Ile Ser Pro Leu Lys
85 90 95
Glu Leu Val Cys Ala Gly Glu Cys Leu Pro Leu Pro Val Leu Pro Asn
100 105 110
Trp Ile Gly Gly Gly Tyr Gly Thr Lys Tyr Trp Ser Arg Arg Ser Ser
115 120 125
Gln Glu Trp Arg Cys Val Asn Asp Lys Thr Arg Thr Gln Arg Ile Gln
130 135 140
Leu Gln Cys Gln Asp Gly Ser Thr Arg Thr Tyr Lys Ile Thr Val Val
145 150 155 160
Thr Ala Cys Lys Cys Lys Arg Tyr Thr Arg Gln His Asn Glu Ser Ser
165 170 175
His Asn Phe Glu Ser Val Ser Pro Ala Lys Pro Ala Gln His His Arg
180 185 190
Glu Arg Lys Arg Ala Ser Lys Ser Ser Lys His Ser Leu Ser
195 200 205

<210> 160
<211> 169
<212> PRT
<213> mouse

<400> 160
Met Ser Gly Leu Arg Thr Leu Leu Gly Leu Gly Leu Leu Val Ala Gly
1 5 10 15
Ser Arg Leu Pro Arg Val Ile Ser Gln Gln Ser Val Cys Arg Ala Arg
20 25 30
Pro Ile Trp Trp Gly Thr Gln Arg Arg Gly Ser Glu Thr Met Ala Gly

```
        35                  40                  45
Ala Ala Val Lys Tyr Leu Ser Gln Glu Glu Ala Gln Ala Val Asp Gln
    50                  55                  60
Glu Leu Phe Asn Glu Tyr Gln Phe Ser Val Asp Gln Leu Met Glu Leu
65                  70                  75                  80
Ala Gly Leu Ser Cys Ala Thr Ala Ile Ala Lys Ala Tyr Pro Pro Thr
                85                  90                  95
Ser Met Ser Lys Ser Pro Pro Thr Val Leu Val Ile Cys Gly Pro Gly
            100                 105                 110
Asn Asn Gly Gly Asp Gly Leu Val Cys Ala Arg His Leu Lys Leu Phe
        115                 120                 125
Gly Tyr Gln Pro Thr Ile Tyr Tyr Pro Lys Arg Pro Asn Lys Pro Leu
    130                 135                 140
Phe Thr Gly Leu Val Thr Gln Cys Gln Lys Met Asp Ile Pro Phe Leu
145                 150                 155                 160
Gly Glu Met Pro Pro Glu Asp Gly Met
                165

<210> 161
<211> 114
<212> PRT
<213> mouse

<400> 161
Met Ser Val Thr Ile Gly Arg Leu Ala Leu Phe Leu Ile Gly Ile Leu
 1               5                  10                  15
Leu Cys Pro Val Ala Pro Ser Leu Thr Arg Ser Trp Pro Gly Pro Asp
            20                  25                  30
Thr Cys Ser Leu Phe Leu Gln His Ser Leu Ser Leu Ser Leu Arg Leu
        35                  40                  45
Gly Gln Ser Leu Glu Gly Gly Leu Ser Val Cys Phe His Val Cys Ile
    50                  55                  60
His Ala Cys Glu Cys Val Ala Cys Cys Arg Val Leu Trp Asp Pro Lys
65                  70                  75                  80
Pro Arg Gly Ser Ser Leu Cys Arg Trp Val Leu Gly Ser Ile Thr Cys
                85                  90                  95
Leu Phe Met Tyr Glu Val Gly Gly Trp Thr Gln Gly Gly Leu Ile Val
            100                 105                 110
Ser Leu

<210> 162
<211> 46
<212> PRT
<213> mouse

<400> 162
Met His Tyr Pro Cys Leu Ala Cys Leu Phe Val Asn Val His Trp Cys
 1               5                  10                  15
Phe Ala Trp Met Cys Ile Leu Val Lys Met Ser Glu Leu Leu Glu Leu
            20                  25                  30
Glu Leu Glu Thr Met Val Ser Cys Leu Val Asp Val Gly Asn
        35                  40                  45

<210> 163
<211> 122
<212> PRT
<213> mouse

<400> 163
Met Phe Thr Phe Val Val Leu Val Ile Thr Ile Val Ile Cys Leu Cys
```

```
1               5                   10                  15
His Val Cys Phe Gly His Phe Lys Tyr Leu Ser Ala His Asn Tyr Lys
            20                  25                  30
Ile Glu His Thr Glu Thr Asp Ala Val Ser Ser Arg Ser Asn Gly Arg
        35                  40                  45
Pro Pro Thr Ala Gly Ala Val Pro Lys Ser Ala Lys Tyr Ile Ala Gln
    50                  55                  60
Val Leu Gln Asp Ser Glu Gly Asp Gly Asp Gly Asp Gly Ala Pro Gly
65                  70                  75                  80
Ser Ser Gly Asp Glu Pro Pro Ser Ser Ser Ser Gln Asp Glu Glu Leu
                85                  90                  95
Leu Met Pro Pro Asp Gly Leu Thr Asp Thr Asp Phe Gln Ser Cys Glu
            100                 105                 110
Asp Ser Leu Ile Glu Asn Glu Ile His Gln
        115                 120

      &lt;210&gt; 164
      &lt;211&gt; 60
      &lt;212&gt; PRT
      &lt;213&gt; Rat

      &lt;400&gt; 164
Met Ser Phe Val Lys Ile Glu Ala Thr Pro Thr Gln Thr Lys Trp Pro
1               5                   10                  15
Phe Ser Val Val Pro Gln Ser Leu Leu Val Thr Val Tyr Ile Cys Tyr
            20                  25                  30
Ile Phe Leu Val Ile Phe Phe Phe Phe Phe Glu Ala Cys Gln Glu Val
        35                  40                  45
Leu Cys Ser Phe Phe Asp Phe Ser Arg Arg Arg Gly
    50                  55                  60

      &lt;210&gt; 165
      &lt;211&gt; 57
      &lt;212&gt; PRT
      &lt;213&gt; mouse

      &lt;400&gt; 165
Met Gly Ser Pro Ile Ser Gly Val Cys Pro Val Leu Pro Gly Gly Leu
1               5                   10                  15
Phe Val Ala Leu Gly Trp Ile Phe Leu Leu Phe His Arg Asp Ala Phe
            20                  25                  30
Ser Leu His Thr Met Ser Ala Gly Phe Pro Lys Ser Pro Ala Asn Pro
        35                  40                  45
His His Pro Pro Leu Arg Leu Ser Pro
    50                  55

      &lt;210&gt; 166
      &lt;211&gt; 75
      &lt;212&gt; PRT
      &lt;213&gt; mouse

      &lt;400&gt; 166
Lys Thr Arg Arg Thr Leu Thr Gly Gln Leu Gly Leu Phe Ser Val Asp
1               5                   10                  15
Phe Met Val Cys Ile Phe Leu Phe Leu Phe Phe Cys Phe Leu Phe Pro
            20                  25                  30
Phe Pro Leu Phe Leu Val Arg Lys His Ile Leu Leu Ser His Cys Lys
        35                  40                  45
Gln Trp Glu Gly Ser Thr Met Thr His Thr His Thr His Thr His Ile
    50                  55                  60
His Ile His Thr Pro Pro Arg Gln Cys Gln Ser
```

65 70 75

<210> 167
<211> 52
<212> PRT
<213> mouse

<400> 167
Val Arg Ser Leu Glu Gln Leu Gly Leu Phe Ser Val Asp Phe Met Val
1 5 10 15
Cys Ile Phe Leu Phe Leu Phe Phe Cys Phe Leu Phe Pro Phe Pro Leu
20 25 30
Phe Leu Val Arg Lys His Ile Leu Leu Ser His Cys Lys Gln Trp Glu
35 40 45
Gly Ser Thr Met
50

<210> 168
<211> 119
<212> PRT
<213> Rat

<400> 168
Met Leu Gly Ala Thr Ser Leu Ser Trp Pro Trp Val Leu Trp Ala Val
1 5 10 15
Ala Gln Arg Asp Ser Val Asp Ala Ile Gly Met Phe Leu Gly Gly Leu
20 25 30
Val Ala Thr Ile Phe Leu Asp Ile Ile Tyr Ile Ser Ile Phe Tyr Ser
35 40 45
Ser Val Ala Val Gly Asp Thr Gly Arg Phe Ser Ala Gly Met Ala Ile
50 55 60
Phe Ser Leu Leu Leu Gln Ala Leu Leu Leu Leu Pro Arg Leu Pro His
65 70 75 80
Ala Pro Gly Ser Glu Gly Val Ser Ser Arg Ser Ala Arg Ile Ser Ser
85 90 95
Asp Leu Leu Arg Asn Ile Val Pro Thr Arg Gln Leu Thr Arg Gln Thr
100 105 110
His Leu Gln Thr Pro Leu Gln
115

<210> 169
<211> 104
<212> PRT
<213> Rat

<220>

<400> 169
Leu Val Pro Lys Ser Ala Arg Ala Ser Leu Leu Cys Cys Gly Pro Lys
1 5 10 15
Leu Ala Ala Cys Gly Ile Val Leu Ser Ala Trp Gly Val Ile Met Leu
20 25 30
Ile Met Leu Gly Ile Phe Phe Asn Val His Ser Ala Val Xaa Ile Xaa
35 40 45
Asp Val Pro Phe Thr Glu Lys Asp Phe Glu Asn Gly Pro Gln Asn Ile
50 55 60
Tyr Asn Leu Tyr Glu Gln Val Ser Tyr Asn Cys Phe Ile Ala Ala Gly
65 70 75 80
Leu Tyr Leu Leu Xaa Gly Gly Phe Ser Phe Cys Gln Val Arg Leu Asn
85 90 95

Lys Arg Lys Glu Tyr Met Val Arg
100

<210> 170
<211> 123
<212> PRT
<213> Rat

<220>
<221> UNSURE
<222> (27)...(27)

<221> UNSURE
<222> (104)...(104)

<221> UNSURE
<222> (118)...(118)

<400> 170
Met Arg Pro Gly Ala Asp Trp Ala Ala Val Cys Ala Leu Trp Pro Ser
1 5 10 15
Trp Arg Pro Ser Cys Ser Leu Pro Ser Ser Xaa Arg Ile Gln Pro Asp
20 25 30
Glu Leu Trp Leu Tyr Arg Asn Pro Tyr Val Lys Ala Glu Tyr Phe Pro
35 40 45
Thr Gly Pro Met Phe Val Ile Ala Phe Leu Thr Pro Leu Ser Leu Ile
50 55 60
Phe Phe Ala Lys Phe Leu Arg Lys Ala Asp Ala Asp Arg Gln Arg Ala
65 70 75 80
Ser Leu Pro Arg Cys Gln Pro Cys Pro Ser Ala Lys Trp Cys Leu Tyr
85 90 95
Gln His His Lys Thr Asp Ser Xaa Gln Gly His Ala Gln Ile Ala Ser
100 105 110
Thr Glu Cys Ser Pro Xaa Gly Ile Ala His Ser
115 120

<210> 171
<211> 75
<212> PRT
<213> Rat

<400> 171
Ser Ala Gly Val Met Thr Ala Ala Val Phe Phe Gly Cys Ala Phe Ile
1 5 10 15
Ala Phe Gly Pro Ala Leu Ser Leu Tyr Val Phe Thr Ile Ala Thr Asp
20 25 30
Pro Leu Arg Val Ile Phe Leu Ile Ala Gly Ala Phe Phe Trp Leu Val
35 40 45
Ser Leu Leu Leu Ser Ser Val Phe Trp Phe Leu Val Arg Val Ile Thr
50 55 60
Asp Asn Arg Asp Gly Pro Val Gln Asn Tyr Leu
65 70 75

<210> 172
<211> 79
<212> PRT
<213> Human

<400> 172
Lys Thr Ser Tyr His Tyr His Thr Asn Val Glu Glu Leu Thr Ile Pro
1 5 10 15

Glu Thr Arg Asn Asn Leu Tyr Ile Ser Ile Ser Trp Leu Trp Cys Leu
20 25 30
Val Leu Val Leu Leu Ser Thr Met Ile Leu Asn Lys His Gly Trp Met
35 40 45
Lys Ala Asn Ala Tyr Ser Leu Val Pro Ser Ile Ile Tyr Ser Pro Ser
50 55 60
Tyr Leu Lys Leu Leu Leu Arg Leu Tyr Lys Leu Gln Ile Cys Cys
65 70 75

<210> 173
<211> 134
<212> PRT
<213> Human

<220>
<400> 173
Leu Arg Gly Arg Gly Arg Gly Val Cys Ser Gln Glu Ser Phe Gly Gly
1 5 10 15
Cys Cys Val Ser Gly Leu Ile Ala Met Gly Thr Lys Ala Gln Val Glu
20 25 30
Arg Lys Leu Leu Cys Leu Phe Ile Leu Ala Ile Leu Leu Cys Ser Leu
35 40 45
Ala Leu Gly Ser Val Thr Val His Ser Ser Glu Pro Glu Val Arg Ile
50 55 60
Pro Glu Asn Asn Pro Val Lys Leu Ser Cys Ala Tyr Ser Gly Phe Ser
65 70 75 80
Ser Pro Arg Val Glu Trp Lys Phe Asp Gln Gly Asp Thr Thr Arg Leu
85 90 95
Val Cys Tyr Asn Asn Lys Ile Thr Ala Ser Tyr Glu Asp Arg Val Thr
100 105 110
Phe Leu Pro Thr Gly Ile Thr Phe Lys Ser Val Thr Arg Glu Asp Thr
115 120 125
Gly Thr Tyr Thr Cys Met
130

<210> 174
<211> 137
<212> PRT
<213> Human

<400> 174
Ala Trp Ser Arg Pro Arg Tyr Asp Ser Val Leu Ala Leu Ser Ala Ala
1 5 10 15
Leu Gln Ala Thr Arg Ala Leu Met Val Val Ser Leu Val Leu Gly Phe
20 25 30
Leu Ala Met Phe Val Ala Thr Met Gly Met Lys Cys Thr Arg Cys Gly
35 40 45
Gly Asp Asp Lys Val Lys Lys Ala Arg Ile Ala Met Gly Gly Gly Ile
50 55 60
Ile Phe Ile Val Ala Gly Leu Ala Ala Leu Val Ala Cys Ser Trp Tyr
65 70 75 80
Gly His Gln Ile Val Thr Asp Phe Tyr Asn Pro Leu Ile Pro Thr Asn
85 90 95
Ile Lys Tyr Glu Phe Gly Pro Ala Ile Phe Ile Gly Trp Ala Gly Ser
100 105 110
Ala Leu Val Ile Leu Gly Gly Ala Leu Ser Pro Val Pro Val Leu Gly
115 120 125
Ile Arg Ala Gly Leu Gly Thr Cys Pro
130 135

<210> 175

<211> 43
<212> PRT
<213> Human

<400> 175
Met Lys Leu Ser Gly Met Phe Leu Leu Leu Ser Leu Ala Leu Phe Cys
1 5 10 15
Phe Leu Thr Gly Val Phe Ser Gln Gly Gly Gln Val Asp Cys Gly Glu
20 25 30
Ser Arg Thr Pro Arg Pro Thr Ala Leu Gly Asn
35 40

<210> 176
<211> 63
<212> PRT
<213> Rat

<400> 176
Pro Asn Thr Arg Pro Arg Arg His Thr Ala Cys Arg Val Ser Ile Ser
1 5 10 15
Val Phe Tyr Met Leu His Thr Glu Leu Lys Lys Cys Trp Phe Phe Leu
20 25 30
Phe Cys Phe Ser Leu Phe Leu Trp Phe Cys Phe Trp Phe Cys Phe Leu
35 40 45
Leu Pro Arg Phe Asp Tyr Leu Pro Met Pro Ser Thr Arg Pro Arg
50 55 60

<210> 177
<211> 52
<212> PRT
<213> mouse

<400> 177
Met Leu Gln Gly Pro Ala Pro Ser Cys Phe Trp Val Phe Ser Gly Ile
1 5 10 15
Cys Val Phe Trp Asp Phe Ile Phe Ile Ile Phe Phe Asn Val Leu Ser
20 25 30
Leu Gly Asn Arg Glu Ile Ser Ala Lys Asp Phe Ala Asp Gln Pro Ala
35 40 45
Gly Ala Gln Gly
50

<210> 178
<211> 62
<212> PRT
<213> mouse

<400> 178
Val Ser Pro Arg Pro Thr Tyr Pro Ser Thr Ala Ser Ser Met Ala Ala
1 5 10 15
Phe Leu Val Thr Gly Phe Phe Phe Ser Leu Phe Val Val Leu Gly Met
20 25 30
Glu Pro Arg Ala Leu Phe Arg Pro Asp Lys Ala Leu Pro Leu Ser Cys
35 40 45
Ala Lys Pro Thr Ser Leu Cys Val Gln Ser Ser Phe Leu Gly
50 55 60

<210> 179
<211> 123
<212> PRT
<213> mouse

<400> 179

```
Ala Ser Arg Thr Ala Val Met Ser Leu Cys Arg Cys Gln Gln Gly Ser
 1               5                  10                  15
Arg Ser Arg Met Asp Leu Asp Val Val Asn Met Phe Val Ile Ala Gly
            20                  25                  30
Gly Thr Leu Ala Ile Pro Ile Leu Ala Phe Val Ala Ser Phe Leu Leu
        35                  40                  45
Trp Pro Ser Ala Leu Ile Arg Ile Tyr Tyr Trp Tyr Trp Arg Arg Thr
    50                  55                  60
Leu Gly Met Gln Val Arg Tyr Ala His His Glu Asp Tyr Gln Phe Cys
65                  70                  75                  80
Tyr Ser Phe Arg Gly Arg Pro Gly His Lys Pro Ser Ile Leu Met Leu
                85                  90                  95
His Gly Phe Ser Ala His Lys Gly His Val Ala Gln Arg Gly Gln Val
            100                 105                 110
Pro Ser Arg Lys Asn Leu His Phe Gly Cys Val
        115                 120
```

<210> 180
<211> 120
<212> PRT
<213> mouse

<220>
<221> UNSURE
<222> (5)...(5)

<400> 180

```
Ala Arg Arg Arg Xaa Arg Trp Arg Arg Gly Cys Cys Trp Leu Ile Gly
 1               5                  10                  15
Thr Gly Leu Arg Ala Ala Thr Trp Thr Val Leu Cys Ser Pro Asn Ser
            20                  25                  30
Ser Leu Val Val Ala Arg His Thr Lys Ser Phe Pro Pro Lys Lys Pro
        35                  40                  45
Leu Gln Ala Leu Thr Met Ser Ile Met Asp His Ser Pro Thr Thr Gly
    50                  55                  60
Val Val Thr Val Ile Val Ile Leu Ile Ala Ile Ala Ala Leu Gly Gly
65                  70                  75                  80
Leu Ile Leu Gly Cys Trp Cys Tyr Leu Arg Leu Gln Arg Ile Ser Gln
                85                  90                  95
Ser Glu Asp Glu Glu Ser Ile Val Gly Asp Gly Glu Thr Lys Glu Pro
            100                 105                 110
Phe Tyr Trp Cys Ser Thr Leu Leu
        115                 120
```

<210> 181
<211> 60
<212> PRT
<213> mouse

<400> 181

```
Lys Gly Pro Glu Val Ser Cys Cys Ile Lys Tyr Phe Ile Phe Gly Phe
 1               5                  10                  15
Asn Val Ile Phe Trp Phe Leu Gly Ile Thr Phe Leu Gly Ile Gly Leu
            20                  25                  30
Trp Ala Trp Asn Glu Lys Gly Val Leu Ser Asn Ile Ser Ser Ile Thr
        35                  40                  45
Asp Leu Gly Gly Phe Asp Pro Val Trp Leu Phe Leu
    50                  55                  60
```

<210> 182
<211> 72
<212> PRT
<213> mouse

<220>

<400> 182

```
Lys Pro Thr Val Gly Ser Ala Glu Val Ala Ile Ala Val Phe Leu Val
 1              5                  10                  15
Ile Cys Ile Ile Val Val Leu Thr Ile Leu Gly Tyr Cys Phe Phe Lys
            20                  25                  30
Asn Gln Arg Lys Glu Phe His Ser Pro Leu His His Pro Pro Pro Thr
        35                  40                  45
Pro Ala Ser Ser Thr Val Ser Thr Thr Glu Asp Thr Glu His Leu Val
    50                  55                  60
Tyr Asn His Thr Thr Gln Pro Leu
65                  70
```

<210> 183
<211> 771
<212> PRT
<213> Rat

<220>

<400> 183

```
Glu Leu Tyr Leu Asp Gly Asn Gln Phe Thr Leu Val Pro Lys Glu Leu
 1              5                  10                  15
Ser Asn Tyr Lys His Leu Thr Leu Ile Asp Leu Ser Asn Asn Arg Ile
            20                  25                  30
Ser Thr Leu Ser Asn Gln Ser Phe Ser Asn Met Thr Gln Leu Leu Thr
        35                  40                  45
Leu Ile Leu Ser Tyr Asn Arg Leu Arg Cys Ile Pro Pro Arg Thr Phe
    50                  55                  60
Asp Gly Leu Lys Ser Leu Arg Leu Leu Ser Leu His Gly Asn Asp Ile
65                  70                  75                  80
Ser Val Val Pro Glu Gly Ala Phe Gly Asp Leu Ser Ala Leu Ser His
                85                  90                  95
Leu Ala Ile Gly Ala Asn Pro Leu Tyr Cys Asp Cys Asn Met Gln Trp
            100                 105                 110
Leu Ser Asp Trp Val Lys Ser Glu Tyr Lys Glu Pro Gly Ile Ala Arg
        115                 120                 125
Cys Ala Gly Pro Gly Glu Met Ala Asp Lys Leu Leu Leu Thr Thr Pro
    130                 135                 140
Ser Lys Asn Phe Thr Cys Gln Gly Pro Val Asp Val Thr Ile Gln Ala
145                 150                 155                 160
Lys Cys Asn Pro Cys Leu Ser Asn Pro Cys Lys Asn Asp Gly Thr Cys
                165                 170                 175
Asn Asn Asp Pro Val Asp Phe Tyr Arg Cys Thr Cys Pro Tyr Gly Phe
            180                 185                 190
Lys Gly Gln Asp Cys Asp Val Pro Ile His Ala Cys Thr Ser Asn Pro
        195                 200                 205
Cys Lys His Gly Gly Thr Cys His Leu Lys Pro Arg Arg Glu Thr Trp
    210                 215                 220
Ile Trp Cys Thr Cys Ala Asp Gly Phe Glu Gly Glu Ser Cys Asp Ile
225                 230                 235                 240
Asn Ile Asp Asp Cys Glu Asp Asn Asp Cys Glu Asn Asn Ser Thr Cys
                245                 250                 255
```

Val Asp Gly Ile Asn Asn Tyr Thr Cys Leu Cys Pro Pro Glu Tyr Thr
260 265 270
Gly Glu Leu Cys Glu Glu Lys Leu Asp Phe Cys Ala Gln Asp Leu Asn
275 280 285
Pro Cys Gln His Asp Ser Lys Cys Ile Leu Thr Pro Lys Gly Phe Lys
290 295 300
Cys Asp Cys Thr Pro Gly Tyr Ile Gly Glu His Cys Asp Ile Asp Phe
305 310 315 320
Asp Asp Cys Gln Asp Asn Lys Cys Lys Asn Gly Ala His Cys Thr Asp
325 330 335
Ala Val Asn Gly Tyr Thr Cys Val Cys Pro Glu Gly Tyr Ser Gly Leu
340 345 350
Phe Cys Glu Phe Ser Pro Pro Met Val Phe Leu Arg Thr Ser Pro Cys
355 360 365
Asp Asn Phe Asp Cys Gln Asn Gly Ala Gln Cys Ile Ile Arg Val Asn
370 375 380
Glu Pro Ile Cys Gln Cys Leu Pro Gly Tyr Leu Gly Glu Lys Cys Glu
385 390 395 400
Lys Leu Val Ser Val Ser Ile Leu Val Asn Lys Glu Ser Tyr Leu Gln
405 410 415
Ile Pro Ser Ala Lys Val Arg Pro Gln Thr Asn Ile Thr Leu Gln Ile
420 425 430
Ala Thr Asp Glu Asp Ser Gly Ile Leu Leu Tyr Lys Gly Asp Lys Asp
435 440 445
His Ile Ala Val Glu Ser Ile Glu Gly Ile Arg Ala Ser Tyr Asp Thr
450 455 460
Gly Ser His Pro Ala Ser Ala Ile Tyr Ser Val Glu Thr Ile Asn Asp
465 470 475 480
Gly Asn Phe His Ile Val Glu Leu Leu Thr Leu Asp Ser Ser Leu Ser
485 490 495
Leu Ser Val Asp Gly Gly Ser Pro Lys Ile Ile Thr Asn Leu Ser Lys
500 505 510
Gln Ser Thr Leu Asn Phe Asp Ser Pro Leu Tyr Val Gly Gly Met Pro
515 520 525
Gly Lys Asn Asn Val Ala Ser Leu Arg Gln Ala Pro Gly Gln Asn Gly
530 535 540
Thr Ser Phe His Gly Cys Ile Arg Asn Leu Tyr Ile Asn Ser Glu Leu
545 550 555 560
Gln Asp Phe Arg Lys Val Pro Met Gln Thr Gly Ile Leu Pro Gly Cys
565 570 575
Glu Pro Cys His Lys Lys Val Cys Ala His Gly Thr Cys Gln Pro Ser
580 585 590
Ser Gln Ser Gly Phe Thr Cys Glu Cys Glu Glu Gly Trp Met Gly Pro
595 600 605
Leu Cys Asp Gln Arg Thr Asn Asp Pro Cys Leu Gly Asn Lys Cys Val
610 615 620
His Gly Thr Cys Leu Pro Ile Asn Ala Phe Ser Tyr Ser Cys Lys Cys
625 630 635 640
Leu Glu Gly His Gly Gly Val Leu Cys Asp Glu Glu Glu Asp Leu Phe
645 650 655
Asn Pro Leu Pro Gly Asp Gln Val Gln Ala Arg Glu Val Gln Ala Leu
660 665 670
Trp Ala Arg Ala Ala Leu Leu Trp Met Gln Gln Trp Ile His Arg Gly
675 680 685
Gln Leu Thr Gln Arg Ile Ser Cys Arg Gly Glu Arg Ile Arg Asp Tyr
690 695 700
Tyr Gln Ser Ser Arg Val Arg Cys Leu Ser Asn Asp

<210> 184
<211> 340
<212> PRT

<213> mouse

<400> 184

```
Asp Gly Ser Leu Trp Leu Gln Ala Thr Gln Pro Asp Asp Ala Gly His
1               5                   10                  15
Tyr Thr Cys Val Pro Ser Asn Gly Phe Leu His Pro Pro Ser Ala Ser
            20                  25                  30
Ala Tyr Leu Thr Val Leu Tyr Pro Ala Gln Val Thr Val Met Pro Pro
        35                  40                  45
Glu Thr Pro Leu Pro Thr Gly Met Arg Gly Val Ile Arg Cys Pro Val
    50                  55                  60
Arg Ala Asn Pro Pro Leu Leu Phe Val Thr Trp Thr Lys Asp Gly Gln
65                  70                  75                  80
Ala Leu Gln Leu Asp Lys Phe Pro Gly Trp Ser Leu Gly Pro Glu Gly
                85                  90                  95
Ser Leu Ile Ile Ala Leu Gly Asn Glu Asp Ala Leu Gly Glu Tyr Ser
            100                 105                 110
Cys Thr Pro Tyr Asn Ser Leu Gly Thr Ala Gly Pro Ser Pro Val Thr
        115                 120                 125
Arg Val Leu Leu Lys Ala Pro Pro Ala Phe Ile Asp Gln Pro Lys Glu
    130                 135                 140
Glu Tyr Phe Gln Glu Val Gly Arg Glu Leu Leu Ile Pro Cys Ser Ala
145                 150                 155                 160
Arg Gly Asp Pro Pro Pro Ile Val Ser Trp Ala Lys Val Gly Arg Gly
                165                 170                 175
Leu Gln Gly Gln Ala Gln Val Asp Ser Asn Asn Ser Leu Val Leu Arg
            180                 185                 190
Pro Leu Thr Lys Glu Ala Gln Gly Arg Trp Glu Cys Ser Ala Ser Asn
        195                 200                 205
Ala Val Ala Arg Val Thr Thr Ser Thr Asn Val Tyr Val Leu Gly Thr
    210                 215                 220
Ser Pro His Val Val Thr Asn Val Ser Val Val Pro Leu Pro Lys Gly
225                 230                 235                 240
Ala Asn Val Ser Trp Glu Pro Gly Phe Asp Gly Gly Tyr Leu Gln Arg
                245                 250                 255
Phe Ser Val Trp Tyr Thr Pro Leu Ala Lys Arg Pro Asp Arg Ala His
            260                 265                 270
His Asp Trp Val Ser Leu Ala Val Pro Ile Gly Ala Thr His Leu Leu
        275                 280                 285
Val Pro Gly Leu Gln Ala His Ala Gln Tyr Gln Phe Ser Val Leu Ala
    290                 295                 300
Gln Asn Lys Leu Gly Ser Gly Pro Phe Ser Glu Ile Val Leu Ser Ile
305                 310                 315                 320
Pro Glu Gly Leu Pro Thr Thr Pro Ala Ala Pro Gly Leu Pro Ala Thr
                325                 330                 335
Arg Ser Arg Val
            340
```

<210> 185
<211> 536
<212> PRT
<213> mouse

<400> 185

```
Lys Val Glu Gly Glu Gly Arg Gly Arg Trp Ala Leu Gly Leu Leu Arg
1               5                   10                  15
Thr Phe Asp Ala Gly Glu Phe Ala Gly Trp Glu Lys Val Gly Ser Gly
            20                  25                  30
Gly Phe Gly Gln Val Tyr Lys Val Arg His Val His Trp Lys Thr Trp
        35                  40                  45
Leu Ala Ile Lys Cys Ser Pro Ser Leu His Val Asp Asp Arg Glu Arg
```

```
                50                  55                  60
Met Glu Leu Leu Glu Glu Ala Lys Lys Met Glu Met Ala Lys Phe Arg
65                  70                  75                  80
Tyr Ile Leu Pro Val Tyr Gly Ile Cys Gln Glu Pro Val Gly Leu Val
                    85                  90                  95
Met Glu Tyr Met Glu Thr Gly Ser Leu Glu Lys Leu Leu Ala Ser Glu
                100                 105                 110
Pro Leu Pro Trp Asp Leu Arg Phe Arg Ile Val His Glu Thr Ala Val
            115                 120                 125
Gly Met Asn Phe Leu His Cys Met Ser Pro Pro Leu Leu His Leu Asp
    130                 135                 140
Leu Lys Pro Ala Asn Ile Leu Leu Asp Ala His Tyr Gln Met Ser Arg
145                 150                 155                 160
Phe Leu Asp Phe Gly Leu Ala Lys Cys Asn Gly Met Ser His Ser His
                    165                 170                 175
Asp Leu Ser Met Asp Gly Leu Phe Gly Thr Ile Gly Tyr Leu Pro Pro
                180                 185                 190
Glu Arg Ile Arg Glu Lys Ser Arg Leu Phe Asp Thr Lys His Asp Val
            195                 200                 205
Tyr Ser Phe Ala Ile Val Ile Trp Gly Val Leu Thr Gln Asn Asn Pro
    210                 215                 220
Phe Ala Asp Glu Lys Asn Ile Leu His Ile Met Met Lys Val Val Lys
225                 230                 235                 240
Gly His Arg Pro Glu Leu Pro Pro Ile Cys Arg Pro Arg Pro Arg Ala
                    245                 250                 255
Cys Ala Ser Leu Ile Gly Leu Met Gln Arg Cys Trp His Ala Asp Pro
                260                 265                 270
Gln Val Arg Pro Thr Phe Gln Glu Ile Thr Ser Glu Thr Glu Asp Leu
            275                 280                 285
Cys Glu Lys Pro Asp Glu Glu Val Lys Asp Leu Ala His Glu Pro Gly
    290                 295                 300
Glu Lys Ser Ser Leu Glu Ser Lys Ser Glu Ala Arg Pro Glu Ser Ser
305                 310                 315                 320
Arg Leu Lys Arg Ala Ser Ala Pro Pro Phe Asp Asn Asp Cys Ser Leu
                    325                 330                 335
Ser Glu Leu Leu Ser Gln Leu Asp Ser Gly Ile Phe Pro Arg Leu Leu
                340                 345                 350
Lys Gly Pro Glu Glu Leu Ser Arg Ser Ser Ser Glu Cys Lys Leu Pro
            355                 360                 365
Ser Ser Ser Ser Gly Lys Arg Leu Ser Gly Val Ser Ser Val Asp Ser
    370                 375                 380
Ala Phe Ser Ser Arg Gly Ser Leu Ser Leu Ser Phe Glu Arg Glu Ala
385                 390                 395                 400
Ser Thr Gly Asp Leu Gly Pro Thr Asp Ile Gln Lys Lys Lys Leu Val
                    405                 410                 415
Asp Ala Ile Ile Ser Gly Asp Thr Ser Arg Leu Met Lys Ile Leu Gln
                420                 425                 430
Pro Gln Asp Val Asp Leu Val Leu Asp Ser Ser Ala Ser Leu Leu His
            435                 440                 445
Leu Ala Val Glu Ala Gly Gln Glu Glu Cys Val Lys Trp Leu Leu Leu
    450                 455                 460
Asn Asn Ala Asn Pro Asn Leu Thr Asn Arg Lys Gly Ser Thr Pro Leu
465                 470                 475                 480
His Met Ala Val Glu Arg Lys Gly Arg Gly Ile Val Glu Leu Leu Leu
                    485                 490                 495
Ala Arg Lys Thr Ser Val Asn Ala Lys Asp Glu Asp Gln Trp Thr Ala
                500                 505                 510
Leu His Phe Ala Ala Gln Asn Gly Asp Glu Gly Gln His Lys Ala Ala
            515                 520                 525
Ala Arg Glu Glu Cys Phe Cys Gln
    530                 535
```

<210> 186
<211> 337
<212> PRT
<213> Rat

<220>

<400> 186
Arg Phe Gly Tyr Gln Met Asp Glu Gly Asn Gln Cys Val Asp
1   5   10   15
Val Asp Glu Cys Ala Thr Asp Ser His Gln Cys Asn Pro Thr Gln Ile
            20   25   30
Cys Ile Asn Thr Glu Gly Gly Tyr Thr Cys Ser Cys Thr Asp Gly Tyr
        35   40   45
Trp Leu Leu Glu Gly Gln Cys Leu Asp Ile Asp Glu Cys Arg Tyr Gly
    50   55   60
Tyr Cys Gln Gln Leu Cys Ala Asn Val Pro Gly Ser Tyr Ser Cys Thr
65   70   75   80
Cys Asn Pro Gly Phe Thr Leu Asn Asp Asp Gly Arg Ser Cys Gln Asp
                85   90   95
Val Asn Glu Cys Glu Thr Glu Asn Pro Cys Val Gln Thr Cys Val Asn
            100   105   110
Thr Tyr Gly Ser Phe Ile Cys Arg Cys Asp Pro Gly Tyr Glu Leu Glu
        115   120   125
Glu Asp Gly Ile His Cys Ser Asp Met Asp Glu Cys Ser Phe Ser Glu
    130   135   140
Phe Leu Cys Gln His Glu Cys Val Asn Gln Pro Gly Ser Tyr Phe Cys
145   150   155   160
Ser Cys Pro Pro Gly Tyr Val Leu Leu Glu Asp Asn Arg Ser Cys Gln
                165   170   175
Asp Ile Asn Glu Cys Glu His Arg Asn His Thr Cys Thr Pro Leu Gln
            180   185   190
Thr Cys Tyr Asn Leu Gln Gly Gly Phe Lys Cys Ile Asp Pro Ile Val
        195   200   205
Cys Glu Glu Pro Tyr Leu Leu Ile Gly Asp Asn Arg Cys Met Cys Pro
    210   215   220
Ala Glu Asn Thr Gly Cys Arg Asp Gln Pro Phe Thr Ile Leu Phe Arg
225   230   235   240
Asp Met Asp Val Val Ser Gly Arg Ser Val Pro Ala Asp Ile Phe Gln
                245   250   255
Met Gln Ala Thr Thr Arg Tyr Pro Gly Ala Tyr Tyr Ile Phe Gln Ile
            260   265   270
Lys Ser Gly Asn Glu Gly Arg Glu Phe Tyr Met Arg Gln Thr Gly Pro
        275   280   285
Ile Ser Ala Thr Leu Val Met Thr Arg Pro Ile Lys Gly Pro Arg Asp
    290   295   300
Ile Gln Leu Asp Leu Glu Met Ile Thr Val Asn Thr Val Ile Asn Phe
305   310   315   320
Arg Gly Ser Ser Val Ile Arg Leu Arg Ile Tyr Val Ser Gln Tyr Pro
                325   330   335
Phe

<210> 187
<211> 152
<212> PRT
<213> mouse

<400> 187

```
Met Ala Leu Gly Val Leu Ile Ala Val Cys Leu Leu Phe Lys Ala Met
 1               5                  10                  15
Lys Ala Ala Leu Ser Glu Glu Ala Glu Val Ile Pro Pro Ser Thr Ala
            20                  25                  30
Gln Gln Ser Asn Trp Thr Phe Asn Asn Thr Glu Ala Asp Tyr Ile Glu
        35                  40                  45
Glu Pro Val Ala Leu Lys Phe Ser His Pro Cys Leu Glu Asp His Asn
    50                  55                  60
Ser Tyr Cys Ile Asn Gly Ala Cys Ala Phe His His Glu Leu Lys Gln
65                  70                  75                  80
Ala Ile Cys Arg Cys Phe Thr Gly Tyr Thr Gly Gln Arg Cys Glu His
                85                  90                  95
Leu Thr Leu Thr Ser Tyr Ala Val Asp Ser Tyr Glu Lys Tyr Ile Ala
            100                 105                 110
Ile Gly Ile Gly Val Gly Leu Leu Ile Ser Ala Phe Leu Ala Val Phe
        115                 120                 125
Tyr Cys Tyr Ile Arg Lys Arg Cys Ile Asn Leu Lys Ser Pro Tyr Ile
    130                 135                 140
Ile Cys Ser Gly Gly Ser Pro Leu
145                 150

      <210> 188
      <211> 118
      <212> PRT
      <213> Rat

      <220>

      <400> 188
Leu Val Pro Gln Phe Gly Thr Arg Ile Arg Tyr ThrAla Tyr Asp Arg
 1               5                  10                  15
Ala Tyr Asn Arg Ala Ser Cys Lys Phe Ile Val Lys Val Gln Val Arg
            20                  25                  30
Arg Cys Pro Ile Leu Lys Pro Pro Gln His Gly Tyr Leu Thr Cys Ser
        35                  40                  45
Ser Ala Gly Asp Asn Tyr Gly Ala Ile Cys Glu Tyr His Cys Asp Gly
    50                  55                  60
Gly Tyr Glu Arg Gln Gly Thr Pro Ser Arg Val Cys Gln Ser Ser Arg
65                  70                  75                  80
Gln Trp Ser Gly Ser Pro Pro Val Cys Thr Pro Met Lys Ile Asn Val
                85                  90                  95
Asn Val Asn Ser Ala Ala Gly Leu Leu Asp Gln Phe Tyr Glu Lys Gln
            100                 105                 110
Arg Leu Leu Ile Val Ser
        115

      <210> 189
      <211> 299
      <212> PRT
      <213> Human

      <220>

      <400> 189
Met Gly Thr Lys Ala Gln Val Glu Arg Lys Leu Leu Cys Leu Phe Ile
 1               5                  10                  15
Leu Ala Ile Leu Leu Cys Ser Leu Ala Leu Gly Ser Val Thr Val His
            20                  25                  30
Ser Ser Glu Pro Glu Val Arg Ile Pro Glu Asn Asn Pro Val Lys Leu
        35                  40                  45
Ser Cys Ala Tyr Ser Gly Phe Ser Ser Pro Arg Val Glu Trp Lys Phe
```

```
    50                  55                  60
Asp Gln Gly Asp Thr Thr Arg Leu Val Cys Tyr Asn Asn Lys Ile Thr
65                  70                  75                  80
Ala Ser Tyr Glu Asp Arg Val Thr Phe Leu Pro Thr Gly Ile Thr Phe
                85                  90                  95
Lys Ser Val Thr Arg Glu Asp Thr Gly Thr Tyr Thr Cys Met Val Ser
            100                 105                 110
Glu Glu Gly Gly Asn Ser Tyr Gly Glu Val Lys Val Lys Leu Ile Val
        115                 120                 125
Leu Val Pro Pro Ser Lys Pro Thr Val Asn Ile Pro Ser Ser Ala Thr
    130                 135                 140
Ile Gly Asn Arg Ala Val Leu Thr Cys Ser Glu Gln Asp Gly Ser Pro
145                 150                 155                 160
Pro Ser Glu Tyr Thr Trp Phe Lys Asp Gly Ile Val Met Pro Thr Asn
                165                 170                 175
Pro Lys Ser Thr Arg Ala Phe Ser Asn Ser Ser Tyr Val Leu Asn Pro
            180                 185                 190
Thr Thr Gly Glu Leu Val Phe Asp Pro Leu Ser Ala Ser Asp Thr Gly
        195                 200                 205
Glu Tyr Ser Cys Glu Ala Arg Asn Gly Tyr Gly Thr Pro Met Thr Ser
    210                 215                 220
Asn Ala Val Arg Met Glu Ala Val Glu Arg Asn Val Gly Val Ile Val
225                 230                 235                 240
Ala Ala Val Leu Val Thr Leu Ile Leu Leu Gly Ile Leu Val Phe Gly
                245                 250                 255
Ile Trp Phe Ala Tyr Ser Arg Gly His Phe Asp Arg Thr Lys Lys Gly
            260                 265                 270
Thr Ser Ser Lys Lys Val Ile Tyr Ser Gln Pro Ser Ala Arg Ser Glu
        275                 280                 285
Gly Glu Phe Lys Gln Thr Ser Ser Phe Leu Val
    290                 295

      <210> 190
      <211> 91
      <212> PRT
      <213> Human

      <400> 190
Gln Pro Thr Val Phe Trp Pro Lys Thr Ser Ala Lys Lys Gly Asn Trp
 1               5                  10                  15
Val Leu Arg Leu Gly Leu Ser Asn Pro Asp Arg Pro Ala Arg Gln Asn
            20                  25                  30
Asn Trp Phe Leu Pro Ala Ser Arg Glu Ile Pro Glu His Ser Ala Leu
        35                  40                  45
Thr Arg Tyr Pro Ala Gln Ile Arg Gly Cys Trp Pro His Arg Leu Thr
    50                  55                  60
Lys Pro Gln Thr Cys Leu Pro Gln Ala Arg Ser Tyr Leu Ser His Glu
65                  70                  75                  80
Val Thr Gln Ala Thr Arg Thr Cys Pro Gly Gly
                85                  90

      <210> 191
      <211> 89
      <212> PRT
      <213> mouse

      <400> 191
Gly Ala Trp Ala Met Leu Tyr Gly Val Ser Met Leu Cys Val Leu Asp
 1               5                  10                  15
Leu Gly Gln Pro Ser Val Val Glu Glu Pro Gly Cys Gly Pro Gly Lys
            20                  25                  30
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```
Val Gln Asn Gly Ser Gly Asn Asn Thr Arg Cys Cys Ser Leu Tyr Ala
        35                  40                  45
Pro Gly Lys Glu Asp Cys Pro Lys Glu Arg Cys Ile Cys Val Thr Pro
    50                  55                  60
Glu Tyr His Cys Gly Asp Pro Gln Cys Lys Ile Cys Lys His Tyr Pro
65                  70                  75                  80
Cys Gln Pro Gly Gln Arg Val Glu Val
                85

      <210> 192
      <211> 299
      <212> PRT
      <213> mouse

      <220>


      <400> 192
Ala Arg Ala Gly Ala Cys Tyr Cys Pro Ala Gly Phe Leu Gly Ala Asp
 1               5                  10                  15
Cys Ser Leu Ala Cys Pro Gln Gly Arg Phe Gly Pro Ser Cys Ala His
            20                  25                  30
Val Cys Thr Cys Gly Gln Gly Ala Ala Cys Asp Pro Val Ser Gly Thr
        35                  40                  45
Cys Ile Cys Pro Pro Gly Lys Thr Gly Gly His Cys Glu Arg Gly Cys
    50                  55                  60
Pro Gln Asp Arg Phe Gly Lys Gly Cys Glu His Lys Cys Ala Cys Arg
65                  70                  75                  80
Asn Gly Gly Leu Cys His Ala Thr Asn Gly Ser Cys Ser Cys Pro Leu
                85                  90                  95
Gly Trp Met Gly Pro His Cys Glu His Ala Cys Pro Ala Gly Arg Tyr
            100                 105                 110
Gly Ala Ala Cys Leu Leu Glu Cys Ser Cys Gln Asn Asn Gly Ser Cys
        115                 120                 125
Glu Pro Thr Ser Gly Ala Cys Leu Cys Gly Pro Gly Phe Tyr Gly Gln
    130                 135                 140
Ala Cys Glu Asp Thr Cys Pro Ala Gly Phe His Gly Ser Gly Cys Gln
145                 150                 155                 160
Arg Val Cys Glu Cys Gln Gln Gly Ala Pro Cys Asp Pro Val Ser Gly
                165                 170                 175
Arg Cys Leu Cys Pro Ala Gly Phe Arg Gly Gln Phe Cys Glu Arg Gly
            180                 185                 190
Cys Lys Pro Gly Phe Phe Gly Asp Gly Cys Leu Gln Gln Cys Asn Cys
        195                 200                 205
Pro Thr Gly Val Pro Cys Asp Pro Ile Ser Gly Leu Cys Leu Cys Pro
    210                 215                 220
Pro Gly Arg Ala Gly Thr Thr Cys Asp Leu Asp Cys Arg Arg Gly Arg
225                 230                 235                 240
Phe Gly Pro Gly Cys Ala Leu Arg Cys Asp Cys Gly Gly Gly Ala Asp
                245                 250                 255
Cys Asp Pro Ile Ser Gly Gln Cys His Cys Val Asp Ser Tyr Thr Gly
            260                 265                 270
Pro Thr Cys Arg Glu Val Pro Thr Gln Leu Ser Ser Ile Arg Pro Ala
        275                 280                 285
Pro Gln His Ser Ser Ser Lys Ala Met Lys His
    290                 295

      <210> 193
      <211> 314
      <212> PRT
      <213> mouse
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<220>

<400> 193

Glu Glu Pro Cys Asn Asn Gly Ser Glu Ile Leu Ala Tyr Asn Ile Asp
1 5 10 15
Leu Gly Asp Ser Cys Ile Thr Val Gly Asn Thr Thr Thr His Val Met
20 25 30
Lys Asn Leu Leu Pro Glu Thr Thr Tyr Arg Ile Arg Ile Gln Ala Ile
35 40 45
Asn Glu Ile Gly Val Gly Pro Phe Ser Gln Phe Ile Lys Ala Lys Thr
50 55 60
Arg Pro Leu Pro Pro Ser Pro Pro Arg Leu Glu Cys Ala Ala Ser Gly
65 70 75 80
Pro Gln Ser Leu Lys Leu Lys Trp Gly Asp Ser Asn Ser Lys Thr His
85 90 95
Ala Ala Gly Asp Met Val Tyr Thr Leu Gln Leu Glu Asp Arg Asn Lys
100 105 110
Arg Phe Ile Ser Ile Tyr Arg Gly Pro Ser His Thr Tyr Lys Val Gln
115 120 125
Arg Leu Thr Glu Phe Thr Cys Tyr Ser Phe Arg Ile Gln Ala Met Ser
130 135 140
Glu Ala Gly Glu Gly Pro Tyr Ser Glu Thr Tyr Thr Phe Ser Thr Thr
145 150 155 160
Lys Ser Val Pro Pro Thr Leu Lys Ala Pro Arg Val Thr Gln Leu Glu
165 170 175
Gly Asn Ser Cys Glu Ile Phe Trp Glu Thr Val Pro Pro Met Arg Gly
180 185 190
Asp Pro Val Ser Tyr Val Leu Gln Val Leu Val Gly Arg Asp Ser Glu
195 200 205
Tyr Lys Gln Val Tyr Lys Gly Glu Glu Ala Thr Phe Gln Ile Ser Gly
210 215 220
Leu Gln Ser Asn Thr Asp Tyr Arg Phe Arg Val Cys Ala Cys Arg Arg
225 230 235 240
Cys Val Asp Thr SerGln Glu Leu Ser Gly Ala Phe Ser Pro Ser Ala
245 250 255
Ala Phe Met Leu Gln Gln Arg Glu Val Met Leu Thr Gly Asp Leu Gly
260 265 270
Gly Met Glu Glu Ala Lys Met Lys Gly Met Met Pro Thr Asp Glu Gln
275 280 285
Phe Ala Ala Leu Ile Val Leu Gly Phe Ala Thr Leu Ser Ile Leu Phe
290 295 300
Ala Phe Ile Leu Gln Tyr Phe Leu Met Lys
305 310

<210> 194
<211> 109
<212> PRT
<213> mouse

<400> 194

Gly Thr Arg Val Gly Thr Pro Tyr Tyr Met Ser Pro Glu Arg Ile His
1 5 10 15
Glu Asn Gly Tyr Asn Phe Lys Ser Asp Ile Trp Ser Leu Gly Cys Leu
20 25 30
Leu Tyr Glu Met Ala Ala Leu Gln Ser Pro Phe Tyr Gly Asp Lys Met
35 40 45
Asn Leu Tyr Ser Leu Cys Lys Lys Ile Glu Gln Cys Asp Tyr Pro Pro
50 55 60
Leu Pro Ser Asp His Tyr Ser Glu Glu Leu Arg Gln Leu Val Asn Ile
65 70 75 80
Cys Ile Asn Pro Asp Pro Glu Lys Arg Pro Asp Ile Ala Tyr Val Tyr

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                85                  90                  95
Asp Val Ala Lys Arg Met His Ala Cys Thr Ala Ser Thr
            100                 105

    <210> 195
    <211> 237
    <212> PRT
    <213> mouse

    <400> 195
Met Leu Ser Leu Arg Ser Leu Leu Pro His Leu Gly Leu Phe Leu Cys
 1               5                  10                  15
Leu Ala Leu His Leu Ser Pro Ser Leu Ser Ala Ser Asp Asn Gly Ser
            20                  25                  30
Cys Val Val Leu Asp Asn Ile Tyr Thr Ser Asp Ile Leu Glu Ile Ser
        35                  40                  45
Thr Met Ala Asn Val Ser Gly Gly Asp Val Thr Tyr Thr Val Thr Val
    50                  55                  60
Pro Val Asn Asp Ser Val Ser Ala Val Ile Leu Lys Ala Val Lys Glu
65                  70                  75                  80
Asp Asp Ser Pro Val Gly Thr Trp Ser Gly Thr Tyr Glu Lys Cys Asn
                85                  90                  95
Asp Ser Ser Val Tyr Tyr Asn Leu Thr Ser Gln Ser Gln Ser Val Phe
            100                 105                 110
Gln Thr Asn Trp Thr Val Pro Thr Ser Glu Asp Val Thr Lys Val Asn
        115                 120                 125
Leu Gln Val Leu Ile Val Val Asn Arg Thr Ala Ser Lys Ser Ser Val
    130                 135                 140
Lys Met Glu Gln Val Gln Pro Ser Ala Ser Thr Pro Ile Pro Glu Ser
145                 150                 155                 160
Ser Glu Thr Ser Gln Thr Ile Asn Thr Thr Pro Thr Val Asn Thr Ala
                165                 170                 175
Lys Thr Thr Ala Lys Asp Thr Ala Asn Thr Thr Ala Val Thr Thr Ala
            180                 185                 190
Asn Thr Thr Ala Asn Thr Thr Ala Val Thr Thr Ala Lys Thr Thr Ala
        195                 200                 205
Lys Ser Leu Ala Ile Arg Thr Leu Gly Ser Pro Leu Ala Gly Ala Leu
    210                 215                 220
His Ile Leu Leu Val Phe Leu Ile Ser Lys Leu Leu Phe
225                 230                 235

    <210> 196
    <211> 154
    <212> PRT
    <213> Human

    <400> 196
Met Ala Leu Gly Val Pro Ile Ser Val Tyr Leu Leu Phe Asn Ala Met
 1               5                  10                  15
Thr Ala Leu Thr Glu Glu Ala Ala Val Thr Val Thr Pro Pro Ile Thr
            20                  25                  30
Ala Gln Gln Gly Asn Trp Thr Val Asn Lys Thr Glu Ala His Asn Ile
        35                  40                  45
Glu Gly Pro Ile Ala Leu Lys Phe Ser His Leu Cys Leu Glu Asp His
    50                  55                  60
Asn Ser Tyr Cys Ile Asn Gly Ala Cys Ala Phe His His Glu Leu Glu
65                  70                  75                  80
Lys Ala Ile Cys Arg Cys Phe Thr Gly Tyr Thr Gly Glu Arg Cys Glu
                85                  90                  95
His Leu Thr Leu Thr Ser Tyr Ala Val Asp Ser Tyr Glu Lys Tyr Ile
            100                 105                 110
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Ala Ile Gly Ile Gly Val Gly Leu Leu Leu Ser Gly Phe Leu Val Ile
115 120 125
Phe Tyr Cys Tyr Ile Arg Lys Arg Cys Leu Lys Leu Lys Ser Pro Tyr
130 135 140
Asn Val Cys Ser Gly Glu Arg Arg Pro Leu
145 150

<210> 197
<211> 171
<212> PRT
<213> Rat

<400> 197
Met Ala Arg Pro Ala Pro Trp Trp Trp Leu Arg Pro Leu Ala Ala Leu
1 5 10 15
Ala Leu Ala Leu Ala Leu Val Arg Val Pro Ser Ala Arg Ala Gly Gln
20 25 30
Met Pro Arg Pro Ala Glu Arg Gly Pro Pro Val Arg Leu Phe Thr Glu
35 40 45
Glu Glu Leu Ala Arg Tyr Ser Gly Glu Glu Glu Asp Gln Pro Ile Tyr
50 55 60
Leu Ala Val Lys Gly Val Val Phe Asp Val Thr Ser Gly Lys Glu Phe
65 70 75 80
Tyr Gly Arg Gly Ala Pro Tyr Asn Ala Leu Ala Gly Lys Asp Ser Ser
85 90 95
Arg Gly Val Ala Lys Met Ser Leu Asp Pro Ala Asp Leu Thr His Asp
100 105 110
Ile Ser Gly Leu Thr Ala Lys Glu Leu Glu Ala Leu Asp Asp Ile Phe
115 120 125
Ser Lys Val Tyr Lys Ala Lys Tyr Pro Ile Val Gly Tyr Thr Ala Arg
130 135 140
Arg Ile Leu Asn Glu Asp Gly Ser Pro Asn Leu Asp Phe Lys Pro Glu
145 150 155 160
Asp Gln Pro His Phe Asp Ile Lys Asp Glu Phe
165 170

<210> 198
<211> 1399
<212> DNA
<213> Mouse

<400> 198
ggcaaagact tcggcacgag asaacagcaa agcagagctg gctgcagcca ttcactggcc 60
tcgggcgggc gtgccacaga ggcagttgaa gtgaaagtga aagagaaacg ataagagaac 120
ggagaccaca ggtgctaagt gagggtgctc acagaacccc ctcttcagcc agagatcact 180
agcaggggaa ctgtggagaa ggcagccagc aaggaagagc ctgagagtag cctccatggg 240
cttggagccc agctggtatc tgctgctctg tttggctgtc tctggggcag cagggactga 300
ccctcccaca gcgcccacca cagcagaaag acagcggcag cccacggaca tcatcttaga 360
ctgcttcttg gtgacagaag acaggcaccg cggggctttt gccagcagtg ggacagggga 420
gagggccttg cttgtgctga agcaggtacc agtgctggat gatggctccc tggaaggcat 480
cacagatttc caggggagca ctgagaccaa acaggattca cctgttatct ttgaggcctc 540
agtggacttg gtacagattc cccaggcaga ggcgttgctc catgctgact gcagcgggaa 600
ggcagtgacc tgcgagatct ccaagtattt cctccaggcc agacaagagg ccacttttga 660
gaaagcacat tggttcatca gcaacatgca ggtttctaga ggtggcccca gtgtctccat 720
ggtgatgaag actctaagag atgctgaagt tggagctgtc cggcacccta cactgaacct 780
acctctgagt gcccagggca cagtgaagac tcaagtggag ttccaggtga catcagagac 840
ccaaaccctg aaccacctgc tggggtcctc tgtctccctg cactgcagtt tctccatggc 900
accagacctg gacctcactg gcgtggagtg gcggctgcag cataaaggca gcggccagct 960
ggtgtacagc tggaagacag ggcaggggca ggccaagcgc aagggcgcta cactggagcc 1020
tgaggagcta ctcagggctg gaaacgcctc tctcacctta cccaacctca ctctaaagga 1080
tgaggggacc tacatctgcc agatctccac ctctctgtat caagctcaac agatcatgcc 1140

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acttaacatc ctggctcccc ccaaagtaca actgcacttg gcaaacaagg atcctctgcc   1200
ttccctcgtc tgcagcattg ccggctacta tcctctggat gtgggagtga cgtggattcg   1260
agaggagctg ggtggaattc cagcccaagt ctctggtgcc tccttctcca gcctcaggca   1320
gagcacgatg ggaacctaca gcatttcttc cacggtgatg gctgacccag gccccacagg   1380
tgccacttat acctgccaa                                                1399

      <210> 199
      <211> 469
      <212> DNA
      <213> Rat

      <400> 199
ggggcgctgg ccagtcatgg cggagccttg ggctgggcag tttctgcaag ctttgcccgc     60
cacggtgctc ggagcgctgg gcaccctggg cagcgagttt ctgcgggagt gggagacaca    120
agatatgcga gtgactctct tcaagcttct cctgctttgg ttggtgttaa gtctcctggg    180
catccagctg gcgtgggggt tctacgggaa cacagtgacc gggttgtatc accgtccagg    240
gaaatggcag caaatgaagc tctcaaaact cacagagaat aaaggaaggc agcaggagaa    300
gggtctccag agatatcgct gggtctgctg gctcctgtgc tgtaccttgc tgctatccag    360
accccttagg caactgcaga gggcttgggt tgggggactg gagtaccatg atgctcccag    420
ggtgagcctc cactgccctc agccttgcct ccaacagcgt caggtactg                469

      <210> 200
      <211> 529
      <212> DNA
      <213> Rat

      <400> 200
aaagcttcca tcctcaacat gccactagtg acgacactct tctacgcctg cttctatcac     60
tacacggagt ccgaggggac cttcagcagt ccagtcaacc tgaagaaaac attcaagatc    120
ccagacagac agtatgtgct gacagccttg gctgcgcggg ccaagcttag agcctggaat    180
gatgtcgacg ccttgttcac cacaaagaac tggttgggtt acaccaagaa gagagcaccc    240
attggcttcc atcgagttgt ggaaattttg cacaagaaca gtgcccctgt ccagatattg    300
caggaatatg tcaatctggt ggaagatgtg gacacaaagt tgaacttagc cactaagttc    360
aagtgccatg atgttgtcat tgatacttgc cgagacctga aggatcgtca acagttgctt    420
gcatacagga gcaaagtaga taaaggatct gctgaggaag agaaaatcga tgtcatcctc    480
agcagctcgc aaattcgatg gaagaactaa ggttcttttg ctacccaga                529

      <210> 201
      <211> 1230
      <212> DNA
      <213> Rat

      <400> 201
aagaattcgg cacgaggcca tggctggttg ggcgggggcc gagctctcgg tcctgaaccc     60
gctgcgtgcg ctgtggctgt tgctggccgc cgccttcctg ctcgcactgc tgctgcagct    120
ggcgcccgcc aggctgctac cgagctgcgc gctcttccag gacctcatcc gctacgggaa    180
gaccaagcag tccggctcgc ggcgccccgc cgtctgcagg gccttcgacg tccccaagag    240
gtacttttct cacttctacg tcgtctcagt gttatggaat ggctccctgc tctggttcct    300
gtctcagtct ctgttcctgg gagcgccgtt tccaagctgg ctttgggctt tgctcagaac    360
tcttggggtc acgcagttcc aagccctggg gatggagtcc aaggcttctc ggatacaagc    420
aggcgagctg gctctgtcta ccttcttagt gttggtgttc ctctgggtcc atagtcttcg    480
gagactcttc gagtgcttct acgtcagcgt cttctctaac acggccattc acgtcgtgca    540
gtactgtttc gggctggtct actatgtcct tgttggcctg accgtactga gccaagtgcc    600
catgaatgac aagaacgtgt acgctctggg gaagaatcta ctgctacaag ctcggtggtt    660
ccacatcttg ggaatgatga tgttcttctg gtcctctgcc catcagtata agtgccacgt    720
cattctcagc aatctcagga gaaataagaa aggtgtggtc atccactgcc agcacagaat    780
ccccttttgga gactggttcg agtatgtgtc ttctgctaac tacctagcag agctgatgat    840
ctacatctcc atggctgtca ccttcgggct ccacaacgta acctggtggc tggtggtgac    900
ctatgtcttc ttcagccaag ccttgtctgc gttcttcaac cacaggttct acaaaagcac    960
atttgtgtcc tacccaaagc ataggaaagc tttcctcccg ttcttgtttt gaacaggctt   1020
tatggtgaag agcgcagccc aggtgacagg ttcccttcct cgagacgctg agacaggctg   1080
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aagtacactt tctgcagctg gcgcccgcca ggctgctacc gagctgcgcg ctcttccagg 1140
acctcatccg ctacgggaag accaagcagt ccggctcgcg gcgccccgcc gtctgcagcc 1200
cgggggatcc actagttcta gagcgccgcc 1230

<210> 202
<211> 778
<212> DNA
<213> Rat

<400> 202
ctgcaggtcg acactagtgg atccaaagat tcggcacgag ataaggcaca tttgcttcat 60
aaaataaaaa aaaaggaaat ttacttagcc gcatgtcagt cacccaaatt ttgagtgtac 120
aaatgaaatg gaaaacattt attacacaaa tttaattaca attctaggga ataaacatgc 180
aaatcagatg gagctcaatc tgcaggcgct gatcctctcc ccctggtttg cagtctgtgc 240
acctcctgga ttcgcccgcg accaggcagt cagaggcctg gctcttgcag gcaggaggat 300
cactgttgta aagaacagcg tcacatttag cgcatctggc gtagtagcag tttttaacac 360
tttgcgcagg tgcctccctt cccccacccg cgctttgtta ggtctacctc tctaaatctc 420
tgccttcctc gcacagtaag tgacctctcc atgacaaagg gcccccagac agcagttata 480
aatcaatgtg ttttgggttt gtttgtttgt ttgttttgtt ttaaagaaaa acccggccat 540
gcttggtggc acttgccttt aatagtagcg cttggtagac agaggcaagc ggttctctgt 600
aagttcaagg ccagcctggt ctacacagtg agaccgggtc tcaaaaacaa aacaacaaaa 660
aacaactcct attgaatcca ctacaggaag ggggggcgcg gatcactgtc tgcaaactaa 720
agtgacttga gctcctgtca cagcctttcc agcaagggca agcttcttta ttagttat 778

<210> 203
<211> 1123
<212> DNA
<213> Rat

<400> 203
gggccccccc tcgagtcgac gktatcgata agcttgatat cgaattcctg caggtcgaca 60
ctagtggatc caaagaattc ggcacgagcc tgaggcgact acggtgcggg tgccgggtgc 120
cgggtgccta cagccccccat cagcttcccc ggggagattc tgccgatttg tcacgagcca 180
tgctcaggag gcagctcgtc tggtggcacc tgctggcttt gcttttcctc ccattttgcc 240
tgtgtcaaga tgaatacatg gagtctccac aagctggagg actgccccca gactgcagca 300
agtgttgcca tggagattat ggattccgtg gttaccaagg gcccccctgga cccccaggtc 360
ctcctggcat tccaggaaac catggaaaca atggaaataa cggagccact ggccacgaag 420
gggccaaggg tgagaaagga gacaaaggcg acctggggcc tcgaggggaa cgggggcagc 480
atggccccaa aggatagaag ggatacccag gggtgccacc agagctgcag attgcgttca 540
tggcttctct agcgactcac ttcagcaatc agaacagtgg cattatcttc agcagtgttg 600
agaccaacat tggaaacttc ttcgatgtca tgactggtag atttggggcc cccgtatcag 660
gcgtgtattt cttcaccttc agcatgatga agcatgagga cgtggaggaa gtgtatgtgt 720
accttatgca caatggtaac acggtgttca gcatgtacag ctatgaaaca aagggaaaat 780
cagatacatc cagcaaccat gcagtgctga agttggccaa aggagatgaa gtctggctaa 840
gaatgggcaa cggtgccctc catggggacc accagcgctt ctctaccttc gcaggctttc 900
tgctttttga aactaagtga tgaggaagtc aggatagctc catgctaagg gcgatttgta 960
ggtgagctag ggttgttagg atctgagggg tgttggagtt gggcttctct atggagtatt 1020
taactgttac attggtcaca ctgctactca ttctaatggc ataccaatta tgttggatac 1080
tttaggggct aggaagaata gaccacaagg taatattccc aga 1123

<210> 204
<211> 434
<212> DNA
<213> Mouse

<400> 204
accaccaagc agatggaatg ctggcacacc catgcacctg catggcgtca caggtggaag 60
attgttaaaa aattgacatc agaaatattt acagaaatag atacctgttt gaataaagtt 120
agagatgaaa tttttgctaa acttcaaccg aagcttagat gcacattagg tgacatggaa 180
agtcctgtgt ttgcacttcc tgtactgtta aagcttgaac cccatgttga aagcctcttt 240
acatattctt tttcttggaa ttttgaatgt tcccattgtg gacaccagta ccaaaacagg 300

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tgtgtgaaga gtctggtcac ctttaccaat attgttcctg agtggcatcc actcaatgct     360
gcccattttg gtccatgtaa cagctgcaac agtaaatcac aaataagaaa aatggtgttg     420
gaaagagcgt cgcc                                                       434
```

<210> 205
<211> 783
<212> DNA
<213> Mouse

<400> 205

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aattcggcac gaggctagtc gaatgtccgg gctgcggacg ctgctggggc tggggctgct      60
ggttgcgggc tcgcgcctgc cacgggtcat cagccagcag agtgtgtgtc gtgcaaggcc     120
catctggtgg ggaacacagc gccggggctc ggagaccatg gcgggcgctg cggtgaagta     180
cttaagtcag gaggaggctc aggccgtgga ccaagagctt tttaacgagt atcagttcag     240
cgtggatcaa ctcatggagc tggccgggtt gagctgtgcc acggctattg ccaaggctta     300
tccccccacg tctatgtcca agagtccccc gactgtcttg gtcatctgtg gccccggaaa     360
taacggaggg gatgggctgg tctgtgcgcg acacctcaaa ctttttggtt accagccaac     420
tatctattac cccaaaagac ctaacaagcc cctcttcact gggctagtga ctcagtgtca     480
gaaaatggac attcctttcc ttggtgaaat gcccccagag gatgggatgt agagaaggga     540
aaccctagcg gaatccaacc agacttactc atctcactga cggcacccaa gaagtctgca     600
actcacttta ctggccgata tcattacctt gggggtcgct ttgtaccacc tgctctagag     660
aagaagtacc agctgaacct gccatcttac cctgacacag agtgtgtcta ccgtctacag     720
taagggaggt gggtaggcag gattctcaat aaagacttgg tactttctgt cttgaaaaaa     780
aaa                                                                   783
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<210> 206
<211> 480
<212> DNA
<213> Mouse

<400> 206

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aaatgaaaac tcttggarct cgcgcgcctg caggtcgaca ctagtggatc caaagaattc      60
ggcacgagtt aaggttttca gactttattt catggtattt gacattgaca catactgagt     120
tagtaacaag ataccatgca gctccctcta gcctcggatc accgaagcag gaagaaggtc     180
agactgcccc catcccagat ttgcttagtt tgtctcccaa tgtgctggac tttaaagaca     240
gggaatggag aagcagatgg atgcttcagt ttcagtcatt tttggctcta tagtgatctc     300
tgccttcctg tacctgtcct tggctggacc ctgggcagta actgtcactc agatgaggac     360
gatcatcatt acaatggacc aactgaggga tgccctcata ttagaccaat taaaagttgc     420
tgtgagttaa accaggaatg accgcacttc cacatcagaa atcaaacaaa atcaatggtt     480
```

<210> 207
<211> 501
<212> DNA
<213> Mouse

<400> 207

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ctgcaggtcg acactagtgg atccaaagaa ttcggcacga gaatcatggc gccgtcgctg      60
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cagcatcgtt cttatatgcg actaacagaa aaggaagatg aatcattacc aatagatata     180
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gggtaaatgc ggggagccct cccacactgg cagccccagg aggcatctct gcagtctctc    1740
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tatagacctg cagagcgcag ctcagagcct atctgccctc tgtctaatac actcgtaaat    2160
atcactttaa ttatagcact ttgcaggaaa taccccaaaa aaaaaa                  2206
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<210> 220
<211> 376
<212> DNA
<213> Human

<400> 220

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tgctccagcc acagggcccg tgtggtgctg agctgggccg actacctcag aagagtggct     180
cccacagctc tggcgacggc gcttgacgtg ggcttgtcca actggagctt cctgtatgtc     240
accgtctcgc tgtgagtact ggccatgccc tgctgcctcc cttcaggctg aagctgtctg     300
tctgtccagc ggggtgtctg cacacccggc tgctaggcca gccactccac cactctggga     360
ccagcccttg ctctct                                                     376
```

<210> 221
<211> 433
<212> DNA
<213> Human

<400> 221

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ctttctcaga cctgtactag tttaccggtt caagaagctc tcatcacatt tttcacttgt     180
attttacata ttgctattcg ggtaattcaa ataaaatgca ggtcttgtaa aagaataaaa     240
acattgacaa gtatgcatgt gccagggacc aaattagagg gttctttggt gcagttagtc     300
caaattctca gatttgaagg ataatatgta ccaataaaaa aaaaatctgc tgctagacat     360
ttacagcagt gctctgtctt gcttcacatt agaaatcgaa aacagctgtt ctcaacaagc     420
caattttatt ttt                                                        433
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<210> 222
<211> 530
<212> DNA
<213> Human

<400> 222

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atattgactt tgtaagaagt atactcttgg aaataggtgc taagcaaata gtgtttggga     180
cctctaagct tatgtgaccg gagttttact cttttgtcct taattttctc attttctttt     240
gactggtgaa aagttgcagt gtaagttaga atttggctcg aagcctgctt ccttagttga     300
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tcctaatgt taggactcta tataccttca gaggcatgtg tgttgggatt gaaattcaaa      420
ttctgatcat gtgaaaatgg cactagttgt tagaggaagt ctctccttca atctcagcat     480
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<210> 223
<211> 550
<212> DNA
<213> Mouse

<400> 223
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tactgaacat tgtcccaaca gaaagttcct atcgttctcc ttccttcttg gcaggcttca 180
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ggggcctgag agcttgcagg cacttaaagc ttcctggcaa aggggccggc cacaggcaga 420
gggaaaggaa caggtcagag gcgttgctct ggcagaggcg gctcgggctg cccatcgtgt 480
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tccttgcccc 550

<210> 224
<211> 470
<212> DNA
<213> Mouse

<400> 224
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tgcttcctca tcttcactca accttaagca gagttcaaag actcaacttc aacattggtc 360
atctgggtgt gtatttatat gtgaataatg atatcagatc cagagtaaca cctttgctgt 420
cttcttagga tgggtgagtg cacggggctc gggctctttg ctgaatactt 470

<210> 225
<211> 1752
<212> DNA
<213> Rat

<400> 225
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ggagctagcc ag 1752

<210> 226
<211> 2165
<212> DNA
<213> Mouse

<400> 226
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aaaaa 2165

<210> 227
<211> 1348
<212> DNA
<213> Mouse

<220>
<221> unsure
<222> (644)...(644)

<400> 227
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atcctggaca gaaataaaac tggactattg ggaatatttt ggaagtgtgc ccgaattggg 180

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gaacgcaaga gtccttatgt cgccatatgc tgtatagtga tggccttcag catcctcttc   240
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cctccagaaa ataatgggaa gaatggttaa gccatttgtc tctgaacatg gaatgagata   360
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ttgttctatt tttgttgttg ttactgttct tatggattgc attcatattt aaaccctttg   720
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tttgtatcca acatttcttc aggttcagct gaaaatcagt tactgtttca aaacaaagag  1260
gaattaaatc ctagctgaaa actatacata gcatttatta attaattact gggtttaact  1320
gctcttttta aaagtttgaa aaaaaaa                                      1348
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<210> 228
<211> 2296
<212> DNA
<213> Mouse

<220>
<221> unsure
<222> (2255)...(2255)

<400> 228

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aatagctatt tcacagcagt aacagaagct acctgctata ataaagacct caacactgct   180
gaccatgatc agcccagcct ggagcctctt cctcatcggg actaaaattg ggctgttctt   240
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taccaacctt ccaaagtatg tcaaagagtt acatttgcaa gagaataaca taaggactat   540
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<210> 229
<211> 1704
<212> DNA
<213> Rat

<220>

<400> 229

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<210> 230
<211> 2004
<212> DNA
<213> Rat

<400> 230

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gattccgatc tgcagcggga aggagtgtcc cattacaggc tcttccctaa agccctggga     360
cagttgatct ccaagtactc tctgcgggag ctacacctgt cattcacgca aggcttttgg     420
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aggacccgat actgggggcc acccttcctg caggctccat caggtgcaga gctctgggtc      480
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<210> 231
<211> 1397
<212> DNA
<213> Rat

<400> 231

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acgagcggca cgagcggccc cgaagggggc tgcacgggcg acttggcggc gatggctcga      180
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<210> 232
<211> 861

<212> DNA
<213> Rat

<400> 232
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gaagaaaaaa aaaaaacaaa aaaaccaaac agtgggtact caaataagat aggagaaaaa 180
tgagagaaca gacccagttc tcgacccttg cttctcaagg tcctcccacc aggctgccaa 240
agcaagatgg tgttgctctg atccagtcag tattcttttg actttttttt ttaatctcca 300
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tctactcagg atcccgagtg tttctgtaga tgtagattgg aatgtgtcca taacagagag 720
gccagtgaga gacatcccca aggacctgcc aggctttcct tcgctccagg aagacgcacc 780
atcactcaaa aggggtttcc tagaaagaaa gacaagtgac ttaaaaaatc tgccagtggg 840
ttcttgaagt catcgaacct a 861

<210> 233
<211> 445
<212> DNA
<213> Mouse

<400> 233
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ggagcaagtg cgtgagcgga cgtgggcctg gcagctgttg caggagataa aggctctctt 180
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cggccgtatt cccagcccat ctcttactca ctagaagttc ctggaagagt catttatcct 300
cttacctgat gccctttctc ctcaatcaga gtggatccct tctctactac ttgactttgg 360
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tgattgttgg gaaggtcctt ggaga 445

<210> 234
<211> 565
<212> DNA
<213> Human

<400> 234
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tctcgctggt tctgtctacc tggcctggat cctgttcttc gtgctctatg atttctgcat 180
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<210> 235
<211> 476
<212> DNA
<213> Human

<400> 235
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agaaaactgg ttgtcctgga tgtttgaaaa gttggtcgtt gtcatggtgt gttacttcat 180

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tatcaatttt tacaactttt ttcctgaaag cagtttagtc catactttgc actgacatac      420
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      &lt;210&gt; 236
      &lt;211&gt; 607
      &lt;212&gt; DNA
      &lt;213&gt; Human

      &lt;400&gt; 236
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cccgccgagc gaatgtaacc cggccttgga cgacccgacg cggactacat gaacctgctg      120
ggcatgatct tcagcatgtg cggcctcatg cttaagctga agtggtgtgc ttgggtcgct      180
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cactctg                                                                607

      &lt;210&gt; 237
      &lt;211&gt; 513
      &lt;212&gt; DNA
      &lt;213&gt; Mouse

      &lt;400&gt; 237
ttctccatta cctctatgcc taatattcat cagccttcat tactctctag catattcacc       60
ttgattcaac agattcaaac ttcctacagc cttctactga tgtcttacaa gctcttgcct      120
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gtactgtggt ccatgtactt actaatatgt tgctttgtaa ttattttcta gcactctgtg      360
ttacagtttc atatttgtat ttatttccaa aattaaattg taagctcctt gagggcagga      420
ataataactt ttacatttgt atctctgcac ccccgagtgc ctagtatagt gctgagcaca      480
tagtaggcgt ttaataaatg cttgttgaag tat                                   513

      &lt;210&gt; 238
      &lt;211&gt; 944
      &lt;212&gt; DNA
      &lt;213&gt; Rat

      &lt;400&gt; 238
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<210> 239
<211> 386
<212> DNA
<213> Rat

<400> 239
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gcccagattt cttctaccga tgcttc 386

<210> 240
<211> 228
<212> DNA
<213> Rat

<400> 240
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<210> 241
<211> 452
<212> DNA
<213> Human

<400> 241
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<210> 242
<211> 1311
<212> DNA
<213> Mouse

<400> 242
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<210> 243
<211> 399
<212> DNA
<213> Mouse

<400> 243

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<210> 244
<211> 1421
<212> DNA
<213> Mouse

<220>
<221> unsure
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<221> unsure
<222> (1395)...(1395)

<400> 244

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<210> 245
<211> 461
<212> DNA
<213> Mouse

<400> 245
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<213> Mouse

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<211> 2411
<212> DNA
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<212> DNA
<213> Mouse

<400> 257

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```

<210> 258
<211> 946
<212> DNA
<213> Mouse

<400> 258

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gacccctgcc ttggtcacag ctgcaggcac gggacatgca tggcgactgg ggactcctac     180
```

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ccctattgcc tatgccagcc tggcttcagt ggccatcact gtgagcaaga gaatccatgt      360
atgggggaga tagtccgtga agccatccgc cgccagaaag actacgcctc ttgtgccacg      420
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catcttttat tatataaata tatcacaccg tctgagtata tggactatac agtgagttat      840
ttttaccaag ttttgttttg tgttgtgtat ttgttgtgtt tttataaaca gctgtttata      900
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```

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<211> 1018
<212> DNA
<213> Human

<400> 259
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tgggggcccc atgcgagcag cgctgcttca actcctatgg gaccttcctg tgtcgctgcc      180
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```

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<210> 260
<211> 2800
<212> DNA
<213> Mouse

<400> 260
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gagacagctg cattactgtg ggcaacacta ccacacacgt gatgaagaac ctccttccag      120
aaacgacata ccggatcaga attcaggcta tcaatgaaat tggagttgga ccatttagtc      180
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cgtctggtcc tcagagcctg aagctcaagt ggggagacag taactccaag acacatgctg      300
ctggtgacat ggtgtacaca ctacagctgg aagacaggaa caagaggttt atctcaatct      360
accgaggacc cagccacacc tacaaggtcc agagactgac agagtttacc tgctactcct      420
tcaggatcca ggcaatgagc gaggcagggg aggggcctta ctcagaaacc tacaccttca      480
gcacaaccaa aagcgtgcct cccaccctca aagcacctcg agtgacgcag ttagaaggga      540
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```

```
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```

<210> 261
<211> 1335
<212> DNA
<213> Mouse

<400> 261

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caaggaaaaa aaaaa                                                    1335
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<210> 262
<211> 1816
<212> DNA
<213> Mouse

<400> 262
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ctttgagtcc aaggggcttc ctgccgagct gaaatccatc ttcaaactca gtgtctttat 180
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ggacctcagc cacggg 1816

<210> 263
<211> 764
<212> DNA
<213> Mouse

<400> 263
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cgggcggcat cccccggccg ccgcacgcac aggccggcgc cctccttgcc tccctgctcc 180
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gctgtgtgtg aaaggcttcc agatgtgaga tccagctcgc ctgcgcacca gacttcatta 720
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<210> 264
<211> 1697
<212> DNA

<213> Mouse

<400> 264

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```

<210> 265
<211> 159
<212> DNA
<213> Mouse

<220>

<400> 265

```
gttttcttct ccaggctgaa gacctgaacg tcaagttgga aggggagcct tccatgcgga      60
aaccaaagca gcggccgcgg ccggagcccc tcatcatccc caccaaggcg ggcactttca     120
tcgcccctcc tgtctactcc aacatcaccc cttaccaga                            159
```

<210> 266
<211> 292
<212> DNA
<213> Mouse

<400> 266

```
gtggggtccc agacttgcca accaaagggc cattcctggt atatggttct ggcttcagct      60
ctggtggcat ggactatggt atggttggtg gcaaggaggc tgggaccgag tctcgcttca     120
aacagtggac ctcaatgatg gaagggctgc catctgtggc cacacaagaa gccaccatgc     180
acaaaaacgg cgctatagtg gcccctggta agacccgagg aggttcacca tacaaccagt     240
ttgatataat cccaggtgac acactgggtg gccatacggg tcctgctggt ga             292
```

<210> 267
<211> 339
<212> DNA

<213> Mouse

<400> 267

```
ccactgacct tcccagaagg tgacagccgg cggcggatgt tgtcaaggag ccgagatagt      60
ccagcagtgc ctcggtaccc agaagacggg ctgtctcccc ccaaaagacg gcgacattcg     120
atgagaagtc accacagtga tctcacattt tgcgagatta tcctgatgga gatggagtcc     180
catgatgcag cctggccttt cctagagcct gtgaaccctc gcttggtgag tggataccga     240
cgtgtcatca agaaccctat ggatttttcc accatgcgag aacgcctgct ccgtggaggg     300
tacactagct cagaagagtt tgcagctgat gctctgctg                            339
```

<210> 268
<211> 153
<212> DNA
<213> Mouse

<400> 268

```
ctgaagttct ctcatccttg tctggaagac cataatagtt actgcattaa tggagcatgt      60
gcattccacc atgagctgaa gcaagccatt tgcagatgct ttactggtta tacgggacaa     120
cgatgtgagc atttgaccct aacttcgtat gct                                  153
```

<210> 269
<211> 153
<212> DNA
<213> Human

<400> 269

```
ttgaagttct cacacctttg cctggaagat cataacagtt actgcatcaa cggtgcttgt      60
gcattccacc atgagctaga gaaagccatc tgcaggtgtt ttactggtta tactggagaa     120
aggtgtgagc acttgacttt aacttcatat gct                                  153
```

<210> 270
<211> 288
<212> DNA
<213> Human

<400> 270

```
gcggccgcgc tgctcctgct gctgctggcg ctgtacaccg cgcgtgtgga cgggtccaaa      60
tgcaagtgct cccggaaggg acccaagatc cgctacagcg acgtgaagaa gctggaaatg     120
aagccaaagt acccgcactg cgaggagaag atggttatca tcaccaccaa gagcgtgtcc     180
aggtaccgag gtcaggagca ctgcctgcac cccaagctgc agagcaccaa gcgcttcatc     240
aagtggtaca acgcctggaa cgagaagcgc agggtctacg aagaatag                  288
```

<210> 271
<211> 234
<212> DNA
<213> Mouse

<400> 271

```
tccaagtgta agtgttcccg gaaggggccc aagatccgct acagcgacgt gaagaagctg      60
gaaatgaagc caaagtaccc acactgcgag gagaagatgg ttatcgtcac caccaagagc     120
atgtccaggt accggggcca ggagcactgc ctgcacccta agctgcagag caccaaacgc     180
ttcatcaagt ggtacaatgc ctggaacgag aagcgcaggg tctacgaaga atag           234
```

<210> 272
<211> 234
<212> DNA
<213> Human
<400> 272

```
tccaaatgca agtgctcccg gaagggaccc aagatccgct acagcgacgt gaagaagctg      60
gaaatgaagc caaagtaccc gcactgcgag gagaagatgg ttatcatcac caccaagagc     120
gtgtccaggt accgaggtca ggagcactgc ctgcacccca agctgcagag caccaagcgc     180
```

```
ttcatcaagt ggtacaacgc ctggaacgag aagcgcaggg tctacgaaga atag          234

      &lt;210&gt; 273
      &lt;211&gt; 645
      &lt;212&gt; DNA
      &lt;213&gt; Mouse

      &lt;400&gt; 273
atgctgtcgc tccgctcctt gcttccacac ctgggactgt tcctgtgcct ggctctgcac     60
ttatcccccct ccctctctgc cagtgataat gggtcctgcg tggtccttga taacatctac    120
acctccgaca tcttggaaat cagcactatg gctaacgtct ctggtgggga tgtaacctat    180
acagtgacgg tccccgtgaa cgattcagtc agtgccgtga tcctgaaagc agtgaaggag    240
gacgacagcc cagtgggcac ctggagtgga acatatgaga agtgcaacga cagcagtgtc    300
tactataact tgacatccca aagccagtcg gtcttccaga caaactggac agttcctact    360
tccgaggatg tgactaaagt caacctgcag gtcctcatcg tcgtcaatcg cacagcctca    420
aagtcatccg tgaaaatgga acaagtacaa ccctcagcct caacccctat tcctgagagt    480
tctgagacca gccagaccat aaacacgact ccaactgtga acacagccaa gactacagcc    540
aaggacacag ccaacaccac agccgtgacc acagccaata ccacagccaa taccacagcc    600
gtgaccacag ccaagaccac agccaaaagc ctggccatcc gcact                    645

      &lt;210&gt; 274
      &lt;211&gt; 63
      &lt;212&gt; DNA
      &lt;213&gt; Mouse

      &lt;400&gt; 274
gggtacagtg atggttacca agtgtgtagt aggttcggaa gcaaagtgcc tcagtttctg     60
aac                                                                   63

      &lt;210&gt; 275
      &lt;211&gt; 388
      &lt;212&gt; PRT
      &lt;213&gt; Mouse
      &lt;400&gt; 275
Met Gly Leu Glu Pro Ser Trp Tyr Leu Leu Leu Cys Leu Ala Val Ser
 1               5                  10                  15
Gly Ala Ala Gly Thr Asp Pro Pro Thr Ala Pro Thr Thr Ala Glu Arg
            20                  25                  30
Gln Arg Gln Pro Thr Asp Ile Ile Leu Asp Cys Phe Leu Val Thr Glu
        35                  40                  45
Asp Arg His Arg Gly Ala Phe Ala Ser Ser Gly Asp Arg Glu Arg Ala
    50                  55                  60
Leu Leu Val Leu Lys Gln Val Pro Val Leu Asp Asp Gly Ser Leu Glu
65                  70                  75                  80
Gly Ile Thr Asp Phe Gln Gly Ser Thr Glu Thr Lys Gln Asp Ser Pro
                85                  90                  95
Val Ile Phe Glu Ala Ser Val Asp Leu Val Gln Ile Pro Gln Ala Glu
            100                 105                 110
Ala Leu Leu His Ala Asp Cys Ser Gly Lys Ala Val Thr Cys Glu Ile
        115                 120                 125
Ser Lys Tyr Phe Leu Gln Ala Arg Gln Glu Ala Thr Phe Glu Lys Ala
    130                 135                 140
His Trp Phe Ile Ser Asn Met Gln Val Ser Arg Gly Gly Pro Ser Val
145                 150                 155                 160
Ser Met Val Met Lys Thr Leu Arg Asp Ala Glu Val Gly Ala Val Arg
                165                 170                 175
His Pro Thr Leu Asn Leu Pro Leu Ser Ala Gln Gly Thr Val Lys Thr
            180                 185                 190
Gln Val Glu Phe Gln Val Thr Ser Glu Thr Gln Thr Leu Asn His Leu
        195                 200                 205
Leu Gly Ser Ser Val Ser Leu His Cys Ser Phe Ser Met Ala Pro Asp
```

```
    210                 215                 220
Leu Asp Leu Thr Gly Val Glu Trp Arg Leu Gln His Lys Gly Ser Gly
225                 230                 235                 240
Gln Leu Val Tyr Ser Trp Lys Thr Gly Gln Gly Gln Ala Lys Arg Lys
                245                 250                 255
Gly Ala Thr Leu Glu Pro Glu Glu Leu Leu Arg Ala Gly Asn Ala Ser
            260                 265                 270
Leu Thr Leu Pro Asn Leu Thr Leu Lys Asp Glu Gly Thr Tyr Ile Cys
        275                 280                 285
Gln Ile Ser Thr Ser Leu Tyr Gln Ala Gln Gln Ile Met Pro Leu Asn
    290                 295                 300
Ile Leu Ala Pro Pro Lys Val Gln Leu His Leu Ala Asn Lys Asp Pro
305                 310                 315                 320
Leu Pro Ser Leu Val Cys Ser Ile Ala Gly Tyr Tyr Pro Leu Asp Val
                325                 330                 335
Gly Val Thr Trp Ile Arg Glu Glu Leu Gly Gly Ile Pro Ala Gln Val
            340                 345                 350
Ser Gly Ala Ser Phe Ser Ser Leu Arg Gln Ser Thr Met Gly Thr Tyr
        355                 360                 365
Ser Ile Ser Ser Thr Val Met Ala Asp Pro Gly Pro Thr Gly Ala Thr
    370                 375                 380
Tyr Thr Cys Gln
385
```

```
<210> 276
<211> 151
<212> PRT
<213> Rat

<400> 276
Met Ala Glu Pro Trp Ala Gly Gln Phe Leu Gln Ala Leu Pro Ala Thr
 1               5                  10                  15
Val Leu Gly Ala Leu Gly Thr Leu Gly Ser Glu Phe Leu Arg Glu Trp
            20                  25                  30
Glu Thr Gln Asp Met Arg Val Thr Leu Phe Lys Leu Leu Leu Leu Trp
        35                  40                  45
Leu Val Leu Ser Leu Leu Gly Ile Gln Leu Ala Trp Gly Phe Tyr Gly
    50                  55                  60
Asn Thr Val Thr Gly Leu Tyr His Arg Pro Gly Lys Trp Gln Gln Met
65                  70                  75                  80
Lys Leu Ser Lys Leu Thr Glu Asn Lys Gly Arg Gln Gln Glu Lys Gly
                85                  90                  95
Leu Gln Arg Tyr Arg Trp Val Cys Trp Leu Leu Cys Cys Thr Leu Leu
            100                 105                 110
Leu Ser Arg Pro Leu Arg Gln Leu Gln Arg Ala Trp Val Gly Gly Leu
        115                 120                 125
Glu Tyr His Asp Ala Pro Arg Val Ser Leu His Cys Pro Gln Pro Cys
    130                 135                 140
Leu Gln Gln Arg Gln Val Leu
145                 150
```

```
<210> 277
<211> 163
<212> PRT
<213> Rat

<400> 277
Met Pro Leu Val Thr Thr Leu Phe Tyr Ala Cys Phe Tyr His Tyr Thr
 1               5                  10                  15
Glu Ser Glu Gly Thr Phe Ser Ser Pro Val Asn Leu Lys Lys Thr Phe
            20                  25                  30
```

Lys Ile Pro Asp Arg Gln Tyr Val Leu Thr Ala Leu Ala Ala Arg Ala
35 40 45
Lys Leu Arg Ala Trp Asn Asp Val Asp Ala Leu Phe Thr Thr Lys Asn
50 55 60
Trp Leu Gly Tyr Thr Lys Lys Arg Ala Pro Ile Gly Phe His Arg Val
65 70 75 80
Val Glu Ile Leu His Lys Asn Ser Ala Pro Val Gln Ile Leu Gln Glu
85 90 95
Tyr Val Asn Leu Val Glu Asp Val Asp Thr Lys Leu Asn Leu Ala Thr
100 105 110
Lys Phe Lys Cys His Asp Val Val Ile Asp Thr Cys Arg Asp Leu Lys
115 120 125
Asp Arg Gln Gln Leu Leu Ala Tyr Arg Ser Lys Val Asp Lys Gly Ser
130 135 140
Ala Glu Glu Glu Lys Ile Asp Val Ile Leu Ser Ser Ser Gln Ile Arg
145 150 155 160
Trp Lys Asn

<210> 278
<211> 330
<212> PRT
<213> Rat

<400> 278
Met Ala Gly Trp Ala Gly Ala Glu Leu Ser Val Leu Asn Pro Leu Arg
1 5 10 15
Ala Leu Trp Leu Leu Leu Ala Ala Ala Phe Leu Leu Ala Leu Leu Leu
20 25 30
Gln Leu Ala Pro Ala Arg Leu Leu Pro Ser Cys Ala Leu Phe Gln Asp
35 40 45
Leu Ile Arg Tyr Gly Lys Thr Lys Gln Ser Gly Ser Arg Arg Pro Ala
50 55 60
Val Cys Arg Ala Phe Asp Val Pro Lys Arg Tyr Phe Ser His Phe Tyr
65 70 75 80
Val Val Ser Val Leu Trp Asn Gly Ser Leu Leu Trp Phe Leu Ser Gln
85 90 95
Ser Leu Phe Leu Gly Ala Pro Phe Pro Ser Trp Leu Trp Ala Leu Leu
100 105 110
Arg Thr Leu Gly Val Thr Gln Phe Gln Ala Leu Gly Met Glu Ser Lys
115 120 125
Ala Ser Arg Ile Gln Ala Gly Glu Leu Ala Leu Ser Thr Phe Leu Val
130 135 140
Leu Val Phe Leu Trp Val His Ser Leu Arg Arg Leu Phe Glu Cys Phe
145 150 155 160
Tyr Val Ser Val Phe Ser Asn Thr Ala Ile His Val Val Gln Tyr Cys
165 170 175
Phe Gly Leu Val Tyr Tyr Val Leu Val Gly Leu Thr Val Leu Ser Gln
180 185 190
Val Pro Met Asn Asp Lys Asn Val Tyr Ala Leu Gly Lys Asn Leu Leu
195 200 205
Leu Gln Ala Arg Trp Phe His Ile Leu Gly Met Met Met Phe Phe Trp
210 215 220
Ser Ser Ala His Gln Tyr Lys Cys His Val Ile Leu Ser Asn Leu Arg
225 230 235 240
Arg Asn Lys Lys Gly Val Val Ile His Cys Gln His Arg Ile Pro Phe
245 250 255
Gly Asp Trp Phe Glu Tyr Val Ser Ser Ala Asn Tyr Leu Ala Glu Leu
260 265 270
Met Ile Tyr Ile Ser Met Ala Val Thr Phe Gly Leu His Asn Val Thr
275 280 285

```
Trp Trp Leu Val Val Thr Tyr Val Phe Phe Ser Gln Ala Leu Ser Ala
    290                 295                 300
Phe Phe Asn His Arg Phe Tyr Lys Ser Thr Phe Val Ser Tyr Pro Lys
305                 310                 315                 320
His Arg Lys Ala Phe Leu Pro Phe Leu Phe
                325                 330


      <210> 279
      <211> 61
      <212> PRT
      <213> Rat

      <400> 279
Met Glu Asn Ile Tyr Tyr Thr Asn Leu Ile Thr Ile Leu Gly Asn Lys
 1               5                  10                  15
His Ala Asn Gln Met Glu Leu Asn Leu Gln Ala Leu Ile Leu Ser Pro
            20                  25                  30
Trp Phe Ala Val Cys Ala Pro Pro Gly Phe Ala Arg Asp Gln Ala Val
        35                  40                  45
Arg Gly Leu Ala Leu Ala Gly Arg Arg Ile Thr Val Val
    50                  55                  60

      <210> 280
      <211> 105
      <212> PRT
      <213> Rat

      <400> 280
Met Leu Arg Arg Gln Leu Val Trp Trp His Leu Leu Ala Leu Leu Phe
 1               5                  10                  15
Leu Pro Phe Cys Leu Cys Gln Asp Glu Tyr Met Glu Ser Pro Gln Ala
            20                  25                  30
Gly Gly Leu Pro Pro Asp Cys Ser Lys Cys Cys His Gly Asp Tyr Gly
        35                  40                  45
Phe Arg Gly Tyr Gln Gly Pro Pro Gly Pro Pro Gly Pro Pro Gly Ile
    50                  55                  60
Pro Gly Asn His Gly Asn Asn Gly Asn Asn Gly Ala Thr Gly His Glu
65                  70                  75                  80
Gly Ala Lys Gly Glu Lys Gly Asp Lys Gly Asp Leu Gly Pro Arg Gly
                85                  90                  95
Glu Arg Gly Gln His Gly Pro Lys Gly
            100                 105

      <210> 281
      <211> 27
      <212> PRT
      <213> Mouse

      <400> 281
Met Leu Lys Ala Ser Leu His Ile Leu Phe Leu Gly Ile Leu Asn Val
 1               5                  10                  15
Pro Ile Val Asp Thr Ser Thr Lys Thr Gly Val
            20                  25

      <210> 282
      <211> 169
      <212> PRT
      <213> Mouse

      <400> 282
Met Ser Gly Leu Arg Thr Leu Leu Gly Leu Gly Leu Leu Val Ala Gly
```

```
1               5                   10                  15
Ser Arg Leu Pro Arg Val Ile Ser Gln Gln Ser Val Cys Arg Ala Arg
            20                  25                  30
Pro Ile Trp Trp Gly Thr Gln Arg Arg Gly Ser Glu Thr Met Ala Gly
        35                  40                  45
Ala Ala Val Lys Tyr Leu Ser Gln Glu Glu Ala Gln Ala Val Asp Gln
    50                  55                  60
Glu Leu Phe Asn Glu Tyr Gln Phe Ser Val Asp Gln Leu Met Glu Leu
65                  70                  75                  80
Ala Gly Leu Ser Cys Ala Thr Ala Ile Ala Lys Ala Tyr Pro Pro Thr
                85                  90                  95
Ser Met Ser Lys Ser Pro Pro Thr Val Leu Val Ile Cys Gly Pro Gly
            100                 105                 110
Asn Asn Gly Gly Asp Gly Leu Val Cys Ala Arg His Leu Lys Leu Phe
        115                 120                 125
Gly Tyr Gln Pro Thr Ile Tyr Tyr Pro Lys Arg Pro Asn Lys Pro Leu
    130                 135                 140
Phe Thr Gly Leu Val Thr Gln Cys Gln Lys Met Asp Ile Pro Phe Leu
145                 150                 155                 160
Gly Glu Met Pro Pro Glu Asp Gly Met
                165

      <210> 283
      <211> 61
      <212> PRT
      <213> Mouse

      <400> 283
Met Glu Lys Gln Met Asp Ala Ser Val Ser Val Ile Phe Gly Ser Ile
 1               5                  10                  15
Val Ile Ser Ala Phe Leu Tyr Leu Ser Leu Ala Gly Pro Trp Ala Val
            20                  25                  30
Thr Val Thr Gln Met Arg Thr Ile Ile Ile Thr Met Asp Gln Leu Arg
        35                  40                  45
Asp Ala Leu Ile Leu Asp Gln Leu Lys Val Ala Val Ser
    50                  55                  60

      <210> 284
      <211> 131
      <212> PRT
      <213> Mouse

      <400> 284
Met Ala Pro Ser Leu Trp Lys Gly Leu Val Gly Val Gly Leu Phe Ala
 1               5                  10                  15
Leu Ala His Ala Ala Phe Ser Ala Ala Gln His Arg Ser Tyr Met Arg
            20                  25                  30
Leu Thr Glu Lys Glu Asp Glu Ser Leu Pro Ile Asp Ile Val Leu Gln
        35                  40                  45
Thr Leu Leu Ala Phe Ala Val Thr Cys Tyr Gly Ile Val His Ile Ala
    50                  55                  60
Gly Glu Phe Lys Asp Met Asp Ala Thr Ser Glu Leu Lys Asn Lys Thr
65                  70                  75                  80
Phe Asp Thr Leu Arg Asn His Pro Ser Phe Tyr Val Phe Asn His Arg
                85                  90                  95
Gly Arg Val Leu Phe Arg Pro Ser Asp Ala Thr Asn Ser Ser Asn Leu
            100                 105                 110
Asp Ala Leu Ser Ser Asn Thr Ser Leu Lys Leu Arg Lys Phe Asp Ser
        115                 120                 125
Leu Arg Arg
    130
```

<210> 285
<211> 78
<212> PRT
<213> Mouse

<400> 285
Gly Thr Arg Lys Pro Leu Pro Met Glu Ala His Ser Arg Arg Glu Lys
1   5   10   15
Ala Ser Gly Leu Arg Leu Ala Trp His Tyr Glu Cys Ser Gly Val Ser
            20   25   30
Val Trp Trp Met Cys Val Leu Gly Trp Leu Ser Phe Leu Val Phe Leu
        35   40   45
Leu Phe Ser Leu Val Cys Ser Phe Pro Ser Pro Ile Asn His Ser His
    50   55   60
Met Leu Pro Cys Leu Phe Leu Arg Gly Gly Gly Ser Asn Val
65   70   75

<210> 286
<211> 206
<212> PRT
<213> Mouse

<400> 286
Met Leu Pro Pro Ala Ile His Leu Ser Leu Ile Pro Leu Leu Cys Ile
1   5   10   15
Leu Met Arg Asn Cys Leu Ala Phe Lys Asn Asp Ala Thr Glu Ile Leu
            20   25   30
Tyr Ser His Val Val Lys Pro Val Pro Ala His Pro Ser Ser Asn Ser
        35   40   45
Thr Leu Asn Gln Ala Arg Asn Gly Gly Arg His Phe Ser Ser Thr Gly
    50   55   60
Leu Asp Arg Asn Ser Arg Val Gln Val Gly Cys Arg Glu Leu Arg Ser
65   70   75   80
Thr Lys Tyr Ile Ser Asp Gly Gln Cys Thr Ser Ile Ser Pro Leu Lys
                85   90   95
Glu Leu Val Cys Ala Gly Glu Cys Leu Pro Leu Pro Val Leu Pro Asn
            100   105   110
Trp Ile Gly Gly Gly Tyr Gly Thr Lys Tyr Trp Ser Arg Arg Ser Ser
        115   120   125
Gln Glu Trp Arg Cys Val Asn Asp Lys Thr Arg Thr Gln Arg Ile Gln
    130   135   140
Leu Gln Cys Gln Asp Gly Ser Thr Arg Thr Tyr Lys Ile Thr Val Val
145   150   155   160
Thr Ala Cys Lys Cys Lys Arg Tyr Thr Arg Gln His Asn Glu Ser Ser
                165   170   175
His Asn Phe Glu Ser Val Ser Pro Ala Lys Pro Ala Gln His His Arg
            180   185   190
Glu Arg Lys Arg Ala Ser Lys Ser Ser Lys His Ser Leu Ser
        195   200   205

<210> 287
<211> 169
<212> PRT
<213> Mouse

<400> 287
Met Ser Gly Leu Arg Thr Leu Leu Gly Leu Gly Leu Leu Val Ala Gly
1   5   10   15
Ser Arg Leu Pro Arg Val Ile Ser Gln Gln Ser Val Cys Arg Ala Arg
            20   25   30

Pro Ile Trp Trp Gly Thr Gln Arg Arg Gly Ser Glu Thr Met Ala Gly
35 40 45
Ala Ala Val Lys Tyr Leu Ser Gln Glu Glu Ala Gln Ala Val Asp Gln
50 55 60
Glu Leu Phe Asn Glu Tyr Gln Phe Ser Val Asp Gln Leu Met Glu Leu
65 70 75 80
Ala Gly Leu Ser Cys Ala Thr Ala Ile Ala Lys Ala Tyr Pro Pro Thr
85 90 95
Ser Met Ser Lys Ser Pro Pro Thr Val Leu Val Ile Cys Gly Pro Gly
100 105 110
Asn Asn Gly Gly Asp Gly Leu Val Cys Ala Arg His Leu Lys Leu Phe
115 120 125
Gly Tyr Gln Pro Thr Ile Tyr Tyr Pro Lys Arg Pro Asn Lys Pro Leu
130 135 140
Phe Thr Gly Leu Val Thr Gln Cys Gln Lys Met Asp Ile Pro Phe Leu
145 150 155 160
Gly Glu Met Pro Pro Glu Asp Gly Met
165

<210> 288
<211> 114
<212> PRT
<213> Mouse

<400> 288
Met Ser Val Thr Ile Gly Arg Leu Ala Leu Phe Leu Ile Gly Ile Leu
1 5 10 15
Leu Cys Pro Val Ala Pro Ser Leu Thr Arg Ser Trp Pro Gly Pro Asp
20 25 30
Thr Cys Ser Leu Phe Leu Gln His Ser Leu Ser Leu Ser Leu Arg Leu
35 40 45
Gly Gln Ser Leu Glu Gly Gly Leu Ser Val Cys Phe His Val Cys Ile
50 55 60
His Ala Cys Glu Cys Val Ala Cys Cys Arg Val Leu Trp Asp Pro Lys
65 70 75 80
Pro Arg Gly Ser Ser Leu Cys Arg Trp Val Leu Gly Ser Ile Thr Cys
85 90 95
Leu Phe Met Tyr Glu Val Gly Gly Trp Thr Gln Gly Gly Leu Ile Val
100 105 110
Ser Leu

<210> 289
<211> 46
<212> PRT
<213> Mouse

<400> 289
Met His Tyr Pro Cys Leu Ala Cys Leu Phe Val Asn Val His Trp Cys
1 5 10 15
Phe Ala Trp Met Cys Ile Leu Val Lys Met Ser Glu Leu Leu Glu Leu
20 25 30
Glu Leu Glu Thr Met Val Ser Cys Leu Val Asp Val Gly Asn
35 40 45

<210> 290
<211> 199
<212> PRT
<213> Mouse

<400> 290

```
Met Val Leu Pro Thr Val Leu Ile Leu Leu Leu Ser Trp Ala Ala Gly
 1               5                  10                  15
Leu Gly Gly Glu Thr Arg Pro Arg Ala Ala Thr Glu Arg Arg Ser Val
            20                  25                  30
Gly Pro Ser Ala Arg Arg Gly Ala Gly Pro Arg Val Ser Gly Leu Leu
        35                  40                  45
Gly Phe Cys Gln Leu Ser Gln Leu Ala Ser Ala Asp Pro Glu Arg Arg
    50                  55                  60
Ser Pro Arg Ala Ile Val Pro Arg Ala Pro Arg Pro Arg Ser Arg Arg
65                  70                  75                  80
Arg Pro Cys Leu Pro Gly Phe Ser Arg Arg Phe Pro Arg Glu Arg Arg
                85                  90                  95
Ser Pro Gly Gln Pro Pro Ser Arg Thr Pro Gln Pro Pro Gln Pro Cys
            100                 105                 110
Arg Gly Pro Ser Pro Gly Thr Ala Gln Thr Arg Ser Asn Leu Arg Gly
        115                 120                 125
Trp Gln Arg Gly Gly Ser Ile Val Leu Gln Ala Ser Glu Arg Thr Arg
    130                 135                 140
Ala Gly Cys Arg Thr Pro Val Cys Val Ser His Pro Ser Ala Phe Pro
145                 150                 155                 160
Pro Pro Arg Ala Leu Phe Gly Val Phe Val Ala Ser Ala Pro Glu Val
                165                 170                 175
Val Cys Val Cys Val Ser Val Val Leu Ser Val Cys Leu Leu Ser Pro
            180                 185                 190
Arg Gly Lys Thr Leu Val Asp
        195

<210> 291
<211> 568
<212> PRT
<213> Rat

<400> 291
Met Glu Leu Leu Tyr Trp Cys Leu Leu Cys Leu Leu Leu Pro Leu Thr
 1               5                  10                  15
Ser Arg Thr Gln Lys Leu Pro Thr Arg Asp Glu Glu Leu Phe Gln Met
            20                  25                  30
Gln Ile Arg Asp Lys Ala Leu Phe His Asp Ser Ser Val Ile Pro Asp
        35                  40                  45
Gly Ala Glu Ile Ser Ser Tyr Leu Phe Arg Asp Thr Pro Arg Arg Tyr
    50                  55                  60
Phe Phe Met Val Glu Glu Asp Asn Thr Pro Leu Ser Val Thr Val Thr
65                  70                  75                  80
Pro Cys Asp Ala Pro Leu Glu Trp Lys Leu Ser Leu Gln Glu Leu Pro
                85                  90                  95
Glu Glu Ser Ser Ala Asp Gly Ser Gly Asp Pro Glu Pro Leu Asp Gln
            100                 105                 110
Gln Lys Gln Gln Met Thr Asp Val Glu Gly Thr Glu Leu Phe Ser Tyr
        115                 120                 125
Lys Gly Asn Asp Val Glu Tyr Phe Leu Ser Ser Ser Ser Pro Ser Gly
    130                 135                 140
Leu Tyr Gln Leu Glu Leu Leu Ser Thr Glu Lys Asp Thr His Phe Lys
145                 150                 155                 160
Val Tyr Ala Thr Thr Thr Pro Glu Ser Asp Gln Pro Tyr Pro Asp Leu
                165                 170                 175
Pro Tyr Asp Pro Arg Val Asp Val Thr Ser Ile Gly Arg Thr Thr Val
            180                 185                 190
Thr Leu Ala Trp Lys Gln Ser Pro Thr Ala Ser Met Leu Lys Gln Pro
        195                 200                 205
Ile Glu Tyr Cys Val Val Ile Asn Lys Glu His Asn Phe Lys Ser Leu
    210                 215                 220
```

```
Cys Ala Ala Glu Thr Lys Met Ser Ala Asp Asp Ala Phe Met Val Ala
225                 230                 235                 240
Pro Lys Pro Gly Leu Asp Phe Ser Pro Phe Asp Phe Ala His Phe Gly
                245                 250                 255
Phe Pro Thr Asp Asn Leu Gly Lys Asp Arg Ser Phe Leu Ala Lys Pro
            260                 265                 270
Ser Pro Lys Val Gly Arg His Val Tyr Trp Arg Pro Lys Val Asp Ile
        275                 280                 285
Lys Lys Ile Cys Ile Gly Ser Lys Asn Ile Phe Thr Val Ser Asp Leu
    290                 295                 300
Lys Pro Asn Thr Gln Tyr Tyr Phe Asp Val Phe Met Val Asn Thr Asn
305                 310                 315                 320
Thr Asn Met Asn Thr Ala Phe Val Gly Ala Phe Ala Arg Thr Lys Glu
                325                 330                 335
Glu Ala Lys Gln Lys Thr Val Glu Leu Lys Asp Gly Arg Val Thr Asp
            340                 345                 350
Val Val Val Lys Arg Lys Gly Lys Lys Phe Leu Arg Phe Ala Pro Val
        355                 360                 365
Ser Ser His Gln Lys Val Thr Leu Phe Ile His Ser Cys Met Asp Thr
    370                 375                 380
Val Gln Val Gln Val Arg Arg Asp Gly Lys Leu Leu Leu Ser Gln Asn
385                 390                 395                 400
Val Glu Gly Ile Arg Gln Phe Gln Leu Arg Gly Lys Pro Lys Gly Lys
                405                 410                 415
Tyr Leu Ile Arg Leu Lys Gly Asn Lys Lys Gly Ala Ser Met Leu Lys
            420                 425                 430
Ile Leu Ala Thr Thr Arg Pro Ser Lys His Ala Phe Pro Ser Leu Pro
        435                 440                 445
Asp Asp Thr Arg Ile Lys Ala Phe Asp Lys Leu Arg Thr Cys Ser Ser
    450                 455                 460
Val Thr Val Ala Trp Leu Gly Thr Gln Glu Arg Arg Lys Phe Cys Ile
465                 470                 475                 480
Tyr Arg Lys Glu Val Gly Gly Asn Tyr Ser Glu Glu Gln Lys Arg Arg
                485                 490                 495
Glu Arg Asn Gln Cys Leu Gly Pro Asp Thr Arg Lys Lys Ser Glu Lys
            500                 505                 510
Val Leu Cys Lys Tyr Phe His Ser Gln Asn Leu Gln Lys Ala Val Thr
        515                 520                 525
Thr Glu Thr Ile Arg Asp Leu Gln Pro Gly Lys Ser Tyr Leu Leu Asp
    530                 535                 540
Val Tyr Val Val Gly His Gly Gly His Ser Val Lys Tyr Gln Ser Lys
545                 550                 555                 560
Leu Val Lys Thr Arg Lys Val Cys
                565

<210> 292
<211> 123
<212> PRT
<213> Mouse

<400> 292
Met Leu Thr Glu Pro Ala Gln Leu Phe Val His Lys Lys Asn Gln Pro
 1               5                  10                  15
Pro Ser His Ser Ser Leu Arg Leu His Phe Arg Thr Leu Ala Gly Ala
            20                  25                  30
Leu Ala Leu Ser Ser Thr Gln Met Ser Trp Gly Leu Gln Ile Leu Pro
        35                  40                  45
Cys Leu Ser Leu Ile Leu Leu Leu Trp Asn Gln Val Pro Gly Leu Glu
    50                  55                  60
Gly Gln Glu Phe Arg Phe Gly Ser Cys Gln Val Thr Gly Val Val Leu
65                  70                  75                  80
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Pro Glu Leu Trp Glu Ala Phe Trp Thr Val Lys Asn Thr Val Gln Thr
85 90 95
Gln Asp Asp Ile Thr Ser Ile Arg Leu Leu Lys Pro Gln Val Leu Arg
100 105 110
Asn Val Ser Val Ile Arg Trp Glu Gly Asp Ser
115 120

<210> 293
<211> 66
<212> PRT
<213> Mouse

<400> 293
Met Asp Val Trp Ser Gly Leu Pro Leu Glu Thr Leu Trp Ile Tyr Glu
1 5 10 15
Ala Val Leu Pro Trp Leu Leu Met Gly Gln Gly His Ala Trp Val Cys
20 25 30
Gly Pro Ile Ala Leu Trp Val Phe Val Asn Val Pro Gly Leu Cys Tyr
35 40 45
His Gln Lys Pro Phe Arg Cys Pro Trp Ser Gly Leu Leu Pro Glu Ala
50 55 60
Leu Cys
65

<210> 294
<211> 294
<212> PRT
<213> Rat

<400> 294
Met Thr Val Phe Arg Lys Val Thr Thr Met Ile Ser Trp Met Leu Leu
1 5 10 15
Ala Cys Ala Leu Pro Cys Ala Ala Asp Pro Met Leu Gly Ala Phe Ala
20 25 30
Arg Arg Asp Phe Gln Lys Gly Gly Pro Gln Leu Val Cys Ser Leu Pro
35 40 45
Gly Pro Gln Gly Pro Pro Gly Pro Pro Gly Ala Pro Gly Ser Ser Gly
50 55 60
Met Val Gly Arg Met Gly Phe Pro Gly Lys Asp Gly Gln Asp Gly Gln
65 70 75 80
Asp Gly Asp Arg Gly Asp Ser Gly Glu Glu Gly Pro Pro Gly Arg Thr
85 90 95
Gly Asn Arg Gly Lys Gln Gly Pro Lys Gly Lys Ala Gly Ala Ile Gly
100 105 110
Arg Ala Gly Pro Arg Gly Pro Lys Gly Val Ser Gly Thr Pro Gly Lys
115 120 125
His Gly Ile Pro Gly Lys Lys Gly Pro Lys Gly Lys Lys Gly Glu Pro
130 135 140
Gly Leu Pro Gly Pro Cys Ser Cys Gly Ser Ser Arg Ala Lys Ser Ala
145 150 155 160
Phe Ser Val Ala Val Thr Lys Ser Tyr Pro Arg Glu Arg Leu Pro Ile
165 170 175
Lys Phe Asp Lys Ile Leu Met Asn Glu Gly Gly His Tyr Asn Ala Ser
180 185 190
Ser Gly Lys Phe Val Cys Ser Val Pro Gly Ile Tyr Tyr Phe Thr Tyr
195 200 205
Asp Ile Thr Leu Ala Asn Lys His Leu Ala Ile Gly Leu Val His Asn
210 215 220
Gly Gln Tyr Arg Ile Arg Thr Phe Asp Ala Asn Thr Gly Asn His Asp
225 230 235 240
Val Ala Ser Gly Ser Thr Ile Leu Ala Leu Lys Glu Gly Asp Glu Val

```
                245                 250                 255
Trp Leu Gln Ile Phe Tyr Ser Glu Gln Asn Gly Leu Phe Tyr Asp Pro
            260                 265                 270
Tyr Trp Thr Asp Ser Leu Phe Thr Gly Phe Leu Ile Tyr Ala Asp Gln
        275                 280                 285
Gly Asp Pro Asn Glu Val
    290

      <210> 295
      <211> 243
      <212> PRT
      <213> Rat

      <400> 295
Met Arg Pro Leu Leu Ala Leu Leu Leu Leu Gly Leu Ala Ser Gly Ser
 1               5                  10                  15
Pro Pro Leu Asp Asp Asn Lys Ile Pro Ser Leu Cys Pro Gly Gln Pro
            20                  25                  30
Gly Leu Pro Gly Thr Pro Gly His His Gly Ser Gln Gly Leu Pro Gly
        35                  40                  45
Arg Asp Gly Arg Asp Gly Arg Asp Gly Ala Pro Gly Ala Pro Gly Glu
    50                  55                  60
Lys Gly Glu Gly Gly Arg Pro Gly Leu Pro Gly Pro Arg Gly Glu Pro
65                  70                  75                  80
Gly Pro Arg Gly Glu Ala Gly Pro Val Gly Ala Ile Gly Pro Ala Gly
                85                  90                  95
Glu Cys Ser Val Pro Pro Arg Ser Ala Phe Ser Ala Lys Arg Ser Glu
            100                 105                 110
Ser Arg Val Pro Pro Pro Ala Asp Thr Pro Leu Pro Phe Asp Arg Val
        115                 120                 125
Leu Leu Asn Glu Gln Gly His Tyr Asp Ala Thr Thr Gly Lys Phe Thr
    130                 135                 140
Cys Gln Val Pro Gly Val Tyr Tyr Phe Ala Val His Ala Thr Val Tyr
145                 150                 155                 160
Arg Ala Ser Leu Gln Phe Asp Leu Val Lys Asn Gly Gln Ser Ile Ala
                165                 170                 175
Ser Phe Phe Gln Phe Phe Gly Gly Trp Pro Lys Pro Ala Ser Leu Ser
            180                 185                 190
Gly Gly Ala Met Val Arg Leu Glu Pro Glu Asp Gln Val Trp Val Gln
        195                 200                 205
Val Gly Val Gly Asp Tyr Ile Gly Ile Tyr Ala Ser Ile Lys Thr Asp
    210                 215                 220
Ser Thr Phe Ser Gly Phe Leu Val Tyr Ser Asp Trp His Ser Ser Pro
225                 230                 235                 240
Val Phe Ala


      <210> 296
      <211> 444
      <212> PRT
      <213> Rat

      <400> 296
Met Leu Val Ala Phe Leu Gly Ala Ser Ala Val Thr Ala Ser Thr Gly
 1               5                  10                  15
Leu Leu Trp Lys Lys Ala His Ala Glu Ser Pro Pro Ser Val Asn Ser
            20                  25                  30
Lys Lys Thr Asp Ala Gly Asp Lys Gly Lys Ser Lys Asp Thr Arg Glu
        35                  40                  45
Val Ser Ser His Glu Gly Ser Ala Ala Asp Thr Ala Ala Glu Pro Tyr
    50                  55                  60
```

Pro Glu Glu Lys Lys Lys Lys Arg Ser Gly Phe Arg Asp Arg Lys Val
65 70 75 80
Met Glu Tyr Glu Asn Arg Ile Arg Ala Tyr Ser Thr Pro Asp Lys Ile
85 90 95
Phe Arg Tyr Phe Ala Thr Leu Lys Val Ile Asn Glu Pro Gly Glu Thr
100 105 110
Glu Val Phe Met Thr Pro Gln Asp Phe Val Arg Ser Ile Thr Pro Asn
115 120 125
Glu Lys Gln Pro Glu His Leu Gly Leu Asp Gln Tyr Ile Ile Lys Arg
130 135 140
Phe Asp Gly Lys Lys Ile Ala Gln Glu Arg Glu Lys Phe Ala Asp Glu
145 150 155 160
Gly Ser Ile Phe Tyr Thr Leu Gly Glu Cys Gly Leu Ile Ser Phe Ser
165 170 175
Asp Tyr Ile Phe Leu Thr Thr Val Leu Ser Thr Pro Gln Arg Asn Phe
180 185 190
Glu Ile Ala Phe Lys Met Phe Asp Leu Asn Gly Asp Gly Glu Val Asp
195 200 205
Met Glu Glu Phe Glu Gln Val Gln Ser Ile Ile Arg Ser Gln Thr Ser
210 215 220
Met Gly Met Arg His Arg Asp Arg Pro Thr Thr Gly Asn Thr Leu Lys
225 230 235 240
Ser Gly Leu Cys Ser Ala Leu Thr Thr Tyr Phe Phe Gly Ala Asp Leu
245 250 255
Lys Gly Lys Leu Thr Ile Lys Asn Phe Leu Glu Phe Gln Arg Lys Leu
260 265 270
Gln His Asp Val Leu Lys Leu Glu Phe Glu Arg His Asp Pro Val Asp
275 280 285
Gly Arg Ile Ser Glu Arg Gln Phe Gly Gly Met Leu Leu Ala Tyr Ser
290 295 300
Gly Val Gln Ser Lys Lys Leu Thr Ala Met Gln Arg Gln Leu Lys Lys
305 310 315 320
His Phe Lys Asp Gly Lys Gly Leu Thr Phe Gln Glu Val Glu Asn Phe
325 330 335
Phe Thr Phe Leu Lys Asn Ile Asn Asp Val Asp Thr Ala Leu Ser Phe
340 345 350
Tyr His Met Ala Gly Ala Ser Leu Asp Lys Val Thr Met Gln Gln Val
355 360 365
Ala Arg Thr Val Ala Lys Val Glu Leu Ser Asp His Val Cys Asp Val
370 375 380
Val Phe Ala Leu Phe Asp Cys Asp Gly Asn Gly Glu Leu Ser Asn Lys
385 390 395 400
Glu Phe Val Ser Ile Met Lys Gln Arg Leu Met Arg Gly Leu Glu Lys
405 410 415
Pro Lys Asp Met Gly Phe Thr Arg Leu Met Gln Ala Met Trp Lys Cys
420 425 430
Ala Gln Glu Thr Ala Trp Asp Phe Ala Leu Pro Lys
435 440

<210> 297
<211> 65
<212> PRT
<213> Human

<400> 297
Met Thr Met Leu His Leu Ala Val Ile Phe Leu Phe Ser Ala Leu Ser
1 5 10 15
Arg Ala Leu Val Gln Cys Ser Ser His Arg Ala Arg Val Val Leu Ser
20 25 30
Trp Ala Asp Tyr Leu Arg Arg Val Ala Pro Thr Ala Leu Ala Thr Ala
35 40 45

Leu Asp Val Gly Leu Ser Asn Trp Ser Phe Leu Tyr Val Thr Val Ser
50 55 60
Leu
65

<210> 298
<211> 52
<212> PRT
<213> Human

<400> 298
Met Lys Ile Asn Ile Ile Gln Gly Ser Ile Met Ile Leu Leu Ile Cys
1 5 10 15
Leu Ser Gln Thr Cys Thr Ser Leu Pro Val Gln Glu Ala Leu Ile Thr
20 25 30
Phe Cys His Leu Tyr Phe Thr Tyr Cys Tyr Ser Gly Asn Ser Asn Lys
35 40 45
Met Gln Val Leu
50

<210> 299
<211> 41
<212> PRT
<213> Human

<400> 299
Met Pro Cys Val Leu Phe Phe Phe Phe Phe Leu Ser Thr Ser Lys Ser
1 5 10 15
Met Ile Tyr Ser Ser Leu Met Leu Gly Leu Tyr Ile Pro Ser Glu Ala
20 25 30
Cys Val Leu Gly Leu Lys Phe Lys Phe
35 40

<210> 300
<211> 80
<212> PRT
<213> Mouse

<400> 300
Met Val Trp Gly Thr Leu Leu Gly Arg Val Leu Ala Ala Leu Leu Asn
1 5 10 15
Ile Val Pro Thr Glu Ser Ser Tyr Arg Ser Pro Ser Phe Leu Ala Gly
20 25 30
Phe Arg Phe Cys Cys Ser Pro Trp Ser Gln His Phe Gly Cys Gly Arg
35 40 45
Leu Thr Ser Cys Leu Pro Pro Cys Val Asp Arg Val Val Lys Thr Tyr
50 55 60
Ser Ser Pro Pro Cys Leu Ser Val Asn Gly His Asp Val Thr Ile Cys
65 70 75 80

<210> 301
<211> 82
<212> PRT
<213> Mouse

<400> 301
Met Gly Ser Val Leu Thr Ser Cys Phe Cys Val Gly Gly Ser Ala Glu
1 5 10 15
Ala Trp Asn Trp Leu Pro Ser Ala Ser Ser Leu Phe Pro Cys Cys Ile
20 25 30
Ala Thr Leu Leu Pro Leu Leu Phe Leu Leu Pro His Leu His Ser Thr

35 40 45
Leu Ser Arg Val Gln Arg Leu Asn Phe Asn Ile Gly His Leu Gly Val
50 55 60
Tyr Leu Tyr Val Asn Asn Asp Ile Arg Ser Arg Val Thr Pro Leu Leu
65 70 75 80
Ser Ser

<210> 302
<211> 411
<212> PRT
<213> Rat

<400> 302
Met Pro Thr Met Trp Pro Leu Leu His Val Leu Trp Leu Ala Leu Val
1 5 10 15
Cys Gly Ser Val His Thr Thr Leu Ser Lys Ser Asp Ala Lys Lys Ala
20 25 30
Ala Ser Lys Thr Leu Leu Glu Lys Thr Gln Phe Ser Asp Lys Pro Val
35 40 45
Gln Asp Arg Gly Leu Val Val Thr Asp Ile Lys Ala Glu Asp Val Val
50 55 60
Leu Glu His Arg Ser Tyr Cys Ser Ala Arg Ala Arg Glu Arg Asn Phe
65 70 75 80
Ala Gly Glu Val Leu Gly Tyr Val Thr Pro Trp Asn Ser His Gly Tyr
85 90 95
Asp Val Ala Lys Val Phe Gly Ser Lys Phe Thr Gln Ile Ser Pro Val
100 105 110
Trp Leu Gln Leu Lys Arg Arg Gly Arg Glu Met Phe Glu Ile Thr Gly
115 120 125
Leu His Asp Val Asp Gln Gly Trp Met Arg Ala Val Lys Lys His Ala
130 135 140
Lys Gly Val Arg Ile Val Pro Arg Leu Leu Phe Glu Asp Trp Thr Tyr
145 150 155 160
Asp Asp Phe Arg Ser Val Leu Asp Ser Glu Asp Glu Ile Glu Glu Leu
165 170 175
Ser Lys Thr Val Val Gln Val Ala Lys Asn Gln His Phe Asp Gly Phe
180 185 190
Val Val Glu Val Trp Ser Gln Leu Leu Ser Gln Lys His Val Gly Leu
195 200 205
Ile His Met Leu Thr His Leu Ala Glu Ala Leu His Gln Ala Arg Leu
210 215 220
Leu Val Ile Leu Val Ile Pro Pro Ala Val Thr Pro Gly Thr Asp Gln
225 230 235 240
Leu Gly Met Phe Thr His Lys Glu Phe Glu Gln Leu Ala Pro Ile Leu
245 250 255
Asp Gly Phe Ser Leu Met Thr Tyr Asp Tyr Ser Thr Ser Gln Gln Pro
260 265 270
Gly Pro Asn Ala Pro Leu Ser Trp Ile Arg Ala Cys Val Gln Val Leu
275 280 285
Asp Pro Lys Ser Gln Trp Arg Ser Lys Ile Leu Leu Gly Leu Asn Phe
290 295 300
Tyr Gly Met Asp Tyr Ala Ala Ser Lys Asp Ala Arg Glu Pro Val Ile
305 310 315 320
Gly Ala Arg Ala Val Leu Lys Val Ala Leu Pro Leu Ala Val Ser Ser
325 330 335
Gln Gln Ile Trp Thr Leu Gly Arg Gly Gly Ser Thr Ser Ala Leu Leu
340 345 350
Leu Ala Gly Leu Gly Leu Ala Ser Glu Pro Cys Thr Lys Ser Glu Glu
355 360 365
Val Pro Lys Lys Ser Leu Leu Asp Thr Val Trp His Trp Gln Gly Glu

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    370                 375                 380
Pro Gly Ala Leu Cys Arg Gly Arg Leu His Thr Trp Ile Leu Val Ser
385                 390                 395                 400
Ala Val Pro Gln Ala Cys Thr Cys Leu Phe Gln
                405                 410

      <210> 303
      <211> 617
      <212> PRT
      <213> Mouse

      <400> 303
Met Gly Ser Pro Arg Leu Ala Ala Leu Leu Leu Ser Leu Pro Leu Leu
 1               5                  10                  15
Leu Ile Gly Leu Ala Val Ser Ala Arg Val Ala Cys Pro Cys Leu Arg
            20                  25                  30
Ser Trp Thr Ser His Cys Leu Leu Ala Tyr Arg Val Asp Lys Arg Phe
        35                  40                  45
Ala Gly Leu Gln Trp Gly Trp Phe Pro Leu Leu Val Arg Lys Ser Lys
    50                  55                  60
Ser Pro Pro Lys Phe Glu Asp Tyr Trp Arg His Arg Thr Pro Ala Ser
65                  70                  75                  80
Phe Gln Arg Lys Leu Leu Gly Ser Pro Ser Leu Ser Glu Glu Ser His
                85                  90                  95
Arg Ile Ser Ile Pro Ser Ser Ala Ile Ser His Arg Gly Gln Arg Thr
            100                 105                 110
Lys Arg Ala Gln Pro Ser Ala Ala Glu Gly Arg Glu His Leu Pro Glu
        115                 120                 125
Ala Gly Ser Gln Lys Cys Gly Gly Pro Glu Phe Ser Phe Asp Leu Leu
    130                 135                 140
Pro Glu Val Gln Ala Val Arg Val Thr Ile Pro Ala Gly Pro Lys Ala
145                 150                 155                 160
Ser Val Arg Leu Cys Tyr Gln Trp Ala Leu Glu Cys Glu Asp Leu Ser
                165                 170                 175
Ser Pro Phe Asp Thr Gln Lys Ile Val Ser Gly Gly His Thr Val Asp
            180                 185                 190
Leu Pro Tyr Glu Phe Leu Leu Pro Cys Met Cys Ile Glu Ala Ser Tyr
        195                 200                 205
Leu Gln Glu Asp Thr Val Arg Arg Lys Lys Cys Pro Phe Gln Ser Trp
    210                 215                 220
Pro Glu Ala Tyr Gly Ser Asp Phe Trp Gln Ser Ile Arg Phe Thr Asp
225                 230                 235                 240
Tyr Ser Gln His Asn Gln Met Val Met Ala Leu Thr Leu Arg Cys Pro
                245                 250                 255
Leu Lys Leu Glu Ala Ser Leu Cys Trp Arg Gln Asp Pro Leu Thr Pro
            260                 265                 270
Cys Glu Thr Leu Pro Asn Ala Thr Ala Gln Glu Ser Glu Gly Trp Tyr
        275                 280                 285
Ile Leu Glu Asn Val Asp Leu His Pro Gln Leu Cys Phe Lys Phe Ser
    290                 295                 300
Phe Glu Asn Ser Ser His Val Glu Cys Pro His Gln Ser Gly Ser Leu
305                 310                 315                 320
Pro Ser Trp Thr Val Ser Met Asp Thr Gln Ala Gln Gln Leu Thr Leu
                325                 330                 335
His Phe Ser Ser Arg Thr Tyr Ala Thr Phe Ser Ala Ala Trp Ser Asp
            340                 345                 350
Pro Gly Leu Gly Pro Asp Thr Pro Met Pro Pro Val Tyr Ser Ile Ser
        355                 360                 365
Gln Thr Gln Gly Ser Val Pro Val Thr Leu Asp Leu Ile Ile Pro Phe
    370                 375                 380
Leu Arg Gln Glu Asn Cys Ile Leu Val Trp Arg Ser Asp Val His Phe
```

385 390 395 400
Ala Trp Lys His Val Leu Cys Pro Asp Asp Ala Pro Tyr Pro Thr Gln
405 410 415
Leu Leu Leu Arg Ser Leu Gly Ser Gly Arg Thr Arg Pro Val Leu Leu
420 425 430
Leu His Ala Ala Asp Ser Glu Ala Gln Arg Arg Leu Val Gly Ala Leu
435 440 445
Ala Glu Leu Leu Arg Thr Ala Leu Gly Gly Gly Arg Asp Val Ile Val
450 455 460
Asp Leu Trp Glu Gly Thr His Val Ala Arg Ile Gly Pro Leu Pro Trp
465 470 475 480
Leu Trp Ala Ala Arg Glu Arg Val Ala Arg Glu Gln Gly Thr Val Leu
485 490 495
Leu Leu Trp Asn Cys Ala Gly Pro Ser Thr Ala Cys Ser Gly Asp Pro
500 505 510
Gln Ala Ala Ser Leu Arg Thr Leu Leu Cys Ala Ala Pro Arg Pro Leu
515 520 525
Leu Leu Ala Tyr Phe Ser Arg Leu Cys Ala Lys Gly Asp Ile Pro Arg
530 535 540
Pro Leu Arg Ala Leu Pro Arg Tyr Arg Leu Leu Arg Asp Leu Pro Arg
545 550 555 560
Leu Leu Arg Ala Leu Asp Ala Gln Pro Ala Thr Leu Ala Ser Ser Trp
565 570 575
Ser His Leu Gly Ala Lys Arg Cys Leu Lys Asn Arg Leu Glu Gln Cys
580 585 590
His Leu Leu Glu Leu Glu Ala Ala Lys Asp Asp Tyr Gln Gly Ser Thr
595 600 605
Asn Ser Pro Cys Gly Phe Ser Cys Leu
610 615

<210> 304
<211> 72
<212> PRT
<213> Mouse

<400> 304
Met Ser Ala Ile Phe Asn Phe Gln Ser Leu Leu Thr Val Ile Leu Leu
1 5 10 15
Leu Ile Cys Thr Cys Ala Tyr Ile Arg Ser Leu Ala Pro Ser Ile Leu
20 25 30
Asp Arg Asn Lys Thr Gly Leu Leu Gly Ile Phe Trp Lys Cys Ala Arg
35 40 45
Ile Gly Glu Arg Lys Ser Pro Tyr Val Ala Ile Cys Cys Ile Val Met
50 55 60
Ala Phe Ser Ile Leu Phe Ile Gln
65 70

<210> 305
<211> 649
<212> PRT
<213> Mouse

<400> 305
Met Ile Ser Pro Ala Trp Ser Leu Phe Leu Ile Gly Thr Lys Ile Gly
1 5 10 15
Leu Phe Phe Gln Val Ala Pro Leu Ser Val Val Ala Lys Ser Cys Pro
20 25 30
Ser Val Cys Arg Cys Asp Ala Gly Phe Ile Tyr Cys Asn Asp Arg Ser
35 40 45
Leu Thr Ser Ile Pro Val Gly Ile Pro Glu Asp Ala Thr Thr Leu Tyr
50 55 60

Leu Gln Asn Asn Gln Ile Asn Asn Val Gly Ile Pro Ser Asp Leu Lys
65 70 75 80
Asn Leu Leu Lys Val Gln Arg Ile Tyr Leu Tyr His Asn Ser Leu Asp
85 90 95
Glu Phe Pro Thr Asn Leu Pro Lys Tyr Val Lys Glu Leu His Leu Gln
100 105 110
Glu Asn Asn Ile Arg Thr Ile Thr Tyr Asp Ser Leu Ser Lys Ile Pro
115 120 125
Tyr Leu Glu Glu Leu His Leu Asp Asp Asn Ser Val Ser Ala Val Ser
130 135 140
Ile Glu Glu Gly Ala Phe Arg Asp Ser Asn Tyr Leu Arg Leu Leu Phe
145 150 155 160
Leu Ser Arg Asn His Leu Ser Thr Ile Pro Gly Gly Leu Pro Arg Thr
165 170 175
Ile Glu Glu Leu Arg Leu Asp Asp Asn Arg Ile Ser Thr Ile Ser Ser
180 185 190
Pro Ser Leu His Gly Leu Thr Ser Leu Lys Arg Leu Val Leu Asp Gly
195 200 205
Asn Leu Leu Asn Asn His Gly Leu Gly Asp Lys Val Phe Phe Asn Leu
210 215 220
Val Asn Leu Thr Glu Leu Ser Leu Val Arg Asn Ser Leu Thr Ala Ala
225 230 235 240
Pro Val Asn Leu Pro Gly Thr Ser Leu Arg Lys Leu Tyr Leu Gln Asp
245 250 255
Asn His Ile Asn Arg Val Pro Pro Asn Ala Phe Ser Tyr Leu Arg Gln
260 265 270
Leu Tyr Arg Leu Asp Met Ser Asn Asn Asn Leu Ser Asn Leu Pro Gln
275 280 285
Gly Ile Phe Asp Asp Leu Asp Asn Ile Thr Gln Leu Ile Leu Arg Asn
290 295 300
Asn Pro Trp Tyr Cys Gly Cys Lys Met Lys Trp Val Arg Asp Trp Leu
305 310 315 320
Gln Ser Leu Pro Val Lys Val Asn Val Arg Gly Leu Met Cys Gln Ala
325 330 335
Pro Glu Lys Val Arg Gly Met Ala Ile Lys Asp Leu Ser Ala Glu Leu
340 345 350
Phe Asp Cys Lys Asp Ser Gly Ile Val Ser Thr Ile Gln Ile Thr Thr
355 360 365
Ala Ile Pro Asn Thr Ala Tyr Pro Ala Gln Gly Gln Trp Pro Ala Pro
370 375 380
Val Thr Lys Gln Pro Asp Ile Lys Asn Pro Lys Leu Ile Lys Asp Gln
385 390 395 400
Arg Thr Thr Gly Ser Pro Ser Arg Lys Thr Ile Leu Ile Thr Val Lys
405 410 415
Ser Val Thr Pro Asp Thr Ile His Ile Ser Trp Arg Leu Ala Leu Pro
420 425 430
Met Thr Ala Leu Arg Leu Ser Trp Leu Lys Leu Gly His Ser Pro Ala
435 440 445
Phe Gly Ser Ile Thr Glu Thr Ile Val Thr Gly Glu Arg Ser Glu Tyr
450 455 460
Leu Val Thr Ala Leu Glu Pro Glu Ser Pro Tyr Arg Val Cys Met Val
465 470 475 480
Pro Met Glu Thr Ser Asn Leu Tyr Leu Phe Asp Glu Thr Pro Val Cys
485 490 495
Ile Glu Thr Gln Thr Ala Pro Leu Arg Met Tyr Asn Pro Thr Thr Thr
500 505 510
Leu Asn Arg Glu Gln Glu Lys Glu Pro Tyr Lys Asn Pro Asn Leu Pro
515 520 525
Leu Ala Ala Ile Ile Gly Gly Ala Val Ala Leu Val Ser Ile Ala Leu
530 535 540
Leu Ala Leu Val Cys Trp Tyr Val His Arg Asn Gly Ser Leu Phe Ser

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545                 550                 555                 560
Arg Asn Cys Ala Tyr Ser Lys Gly Arg Arg Arg Lys Asp Asp Tyr Ala
                565                 570                 575
Glu Ala Gly Thr Lys Lys Asp Asn Ser Ile Leu Glu Ile Arg Glu Thr
            580                 585                 590
Ser Phe Gln Met Leu Pro Ile Ser Asn Glu Pro Ile Ser Lys Glu Glu
        595                 600                 605
Phe Val Ile His Thr Ile Phe Pro Pro Asn Gly Met Asn Leu Tyr Lys
    610                 615                 620
Asn Asn Leu Ser Glu Ser Ser Ser Asn Arg Ser Tyr Arg Asp Ser Gly
625                 630                 635                 640
Ile Pro Asp Ser Asp His Ser His Ser
                645

      <210> 306
      <211> 150
      <212> PRT
      <213> Rat

      <400> 306
Met Ala Ala Pro Met Asp Arg Thr His Gly Gly Arg Ala Ala Arg Ala
 1               5                  10                  15
Leu Arg Arg Ala Leu Ala Leu Ala Ser Leu Ala Gly Leu Leu Leu Ser
            20                  25                  30
Gly Leu Ala Gly Ala Leu Pro Thr Leu Gly Pro Gly Trp Arg Arg Gln
        35                  40                  45
Asn Pro Glu Pro Pro Ala Ser Arg Thr Arg Ser Leu Leu Leu Asp Ala
    50                  55                  60
Ala Ser Gly Gln Leu Arg Leu Glu Tyr Gly Phe His Pro Asp Ala Val
65                  70                  75                  80
Ala Trp Ala Asn Leu Thr Asn Ala Ile Arg Glu Thr Gly Trp Ala Tyr
                85                  90                  95
Leu Asp Leu Gly Thr Asn Gly Ser Tyr Lys Trp Ile Pro Arg Ala Ala
            100                 105                 110
Gly Leu Cys Ser Trp Cys Gly Gly Gly Leu Cys Val Arg Gly Ala His
        115                 120                 125
Leu His Ala Leu Asp Glu His Gly Gly Gln Leu Leu Arg Pro Leu Arg
    130                 135                 140
Val Arg Ser Arg Leu Leu
145                 150

      <210> 307
      <211> 580
      <212> PRT
      <213> Rat

      <400> 307
Met Ala Ala Ala Met Pro Leu Gly Leu Ser Leu Leu Leu Leu Val Leu
 1               5                  10                  15
Val Gly Gln Gly Cys Cys Gly Arg Val Glu Gly Pro Arg Asp Ser Leu
            20                  25                  30
Arg Glu Glu Leu Val Ile Thr Pro Leu Pro Ser Gly Asp Val Ala Ala
        35                  40                  45
Thr Phe Gln Phe Arg Thr Arg Trp Asp Ser Asp Leu Gln Arg Glu Gly
    50                  55                  60
Val Ser His Tyr Arg Leu Phe Pro Lys Ala Leu Gly Gln Leu Ile Ser
65                  70                  75                  80
Lys Tyr Ser Leu Arg Glu Leu His Leu Ser Phe Thr Gln Gly Phe Trp
                85                  90                  95
Arg Thr Arg Tyr Trp Gly Pro Pro Phe Leu Gln Ala Pro Ser Gly Ala
            100                 105                 110
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Glu Leu Trp Val Trp Phe Gln Asp Thr Val Thr Asp Val Asp Lys Ser
        115                 120                 125
Trp Lys Glu Leu Ser Asn Val Leu Ser Gly Ile Phe Cys Ala Ser Leu
    130                 135                 140
Asn Phe Ile Asp Ser Thr Asn Thr Val Thr Pro Thr Ala Ser Phe Lys
145                 150                 155                 160
Pro Leu Gly Leu Ala Asn Asp Thr Asp His Tyr Phe Leu Arg Tyr Ala
                165                 170                 175
Val Leu Pro Arg Glu Val Val Cys Thr Glu Asn Leu Thr Pro Trp Lys
            180                 185                 190
Lys Leu Leu Pro Cys Ser Ser Lys Ala Gly Leu Ser Val Leu Leu Lys
        195                 200                 205
Ala Asp Arg Leu Phe His Thr Ser Tyr His Ser Gln Ala Val His Ile
    210                 215                 220
Arg Pro Ile Cys Arg Asn Ala His Cys Thr Ser Ile Ser Trp Glu Leu
225                 230                 235                 240
Arg Gln Thr Leu Ser Val Val Phe Asp Ala Phe Ile Thr Gly Gln Gly
                245                 250                 255
Lys Lys Asp Trp Ser Leu Phe Arg Met Phe Ser Arg Thr Leu Thr Glu
            260                 265                 270
Ala Cys Pro Leu Ala Ser Gln Ser Leu Val Tyr Val Asp Ile Thr Gly
        275                 280                 285
Tyr Ser Gln Asp Asn Glu Thr Leu Glu Val Ser Pro Pro Pro Thr Ser
    290                 295                 300
Thr Tyr Gln Asp Val Ile Leu Gly Thr Arg Lys Thr Tyr Ala Val Tyr
305                 310                 315                 320
Asp Leu Phe Asp Thr Ala Met Ile Asn Asn Ser Arg Asn Leu Asn Ile
                325                 330                 335
Gln Leu Lys Trp Lys Arg Pro Pro Asp Asn Glu Ala Leu Pro Val Pro
            340                 345                 350
Phe Leu His Ala Gln Arg Tyr Val Ser Gly Tyr Gly Leu Gln Lys Gly
        355                 360                 365
Glu Leu Ser Thr Leu Leu Tyr Asn Ser His Pro Tyr Arg Ala Phe Pro
    370                 375                 380
Val Leu Leu Leu Asp Ala Val Pro Trp Tyr Leu Arg Leu Tyr Val His
385                 390                 395                 400
Thr Leu Thr Ile Thr Ser Lys Gly Lys Asp Asn Lys Pro Ser Tyr Ile
                405                 410                 415
His Tyr Gln Pro Ala Gln Asp Arg Gln Gln Pro His Leu Leu Glu Met
            420                 425                 430
Leu Ile Gln Leu Pro Ala Asn Ser Val Thr Lys Val Ser Ile Gln Phe
        435                 440                 445
Glu Arg Ala Leu Leu Lys Trp Thr Glu Tyr Thr Pro Asp Pro Asn His
    450                 455                 460
Gly Phe Tyr Val Ser Pro Ser Val Leu Ser Ala Leu Val Pro Ser Met
465                 470                 475                 480
Val Ala Ala Lys Pro Val Asp Trp Glu Glu Ser Pro Leu Phe Asn Thr
                485                 490                 495
Leu Phe Pro Val Ser Asp Gly Ser Ser Tyr Phe Val Arg Leu Tyr Thr
            500                 505                 510
Glu Pro Leu Leu Val Asn Leu Pro Thr Pro Asp Phe Ser Met Pro Tyr
        515                 520                 525
Asn Val Ile Cys Leu Thr Cys Thr Val Val Ala Val Cys Tyr Gly Ser
    530                 535                 540
Phe Tyr Asn Leu Leu Thr Arg Thr Phe His Ile Glu Glu Pro Lys Ser
545                 550                 555                 560
Gly Gly Leu Ala Lys Arg Leu Ala Asn Leu Ile Arg Arg Ala Arg Gly
                565                 570                 575
Val Pro Pro Leu
            580
```

<210> 308
<211> 283
<212> PRT
<213> Rat

<400> 308
```
Met Thr Ser Gly Pro Gly Gly Pro Ala Ala Ala Thr Gly Gly Gly Lys
 1               5                  10                  15
Asp Thr His Gln Trp Tyr Val Cys Asn Arg Glu Lys Leu Cys Glu Ser
            20                  25                  30
Leu Gln Ser Val Phe Val Gln Ser Tyr Leu Asp Gln Gly Thr Gln Ile
        35                  40                  45
Phe Leu Asn Asn Ser Ile Glu Lys Ser Gly Trp Leu Phe Ile Gln Leu
    50                  55                  60
Tyr His Ser Phe Val Ser Ser Val Phe Ser Leu Phe Met Ser Arg Thr
65                  70                  75                  80
Ser Ile Asn Gly Leu Leu Gly Arg Gly Ser Met Phe Val Phe Ser Pro
                85                  90                  95
Asp Gln Phe Gln Arg Leu Leu Lys Ile Asn Pro Asp Trp Lys Thr His
            100                 105                 110
Arg Leu Leu Asp Leu Gly Ala Gly Asp Gly Glu Val Thr Lys Ile Met
        115                 120                 125
Ser Pro His Phe Glu Glu Ile Tyr Ala Thr Glu Leu Ser Glu Thr Met
    130                 135                 140
Ile Trp Gln Leu Gln Lys Lys Lys Tyr Arg Val Leu Gly Ile Asn Glu
145                 150                 155                 160
Trp Gln Asn Thr Gly Phe Gln Tyr Asp Val Ile Ser Cys Leu Asn Leu
                165                 170                 175
Leu Asp Arg Cys Asp Gln Pro Leu Thr Leu Leu Lys Asp Ile Arg Ser
            180                 185                 190
Val Leu Glu Pro Thr Gln Gly Arg Val Ile Leu Ala Leu Val Leu Pro
        195                 200                 205
Phe His Pro Tyr Val Glu Asn Val Gly Gly Lys Trp Glu Lys Pro Ser
    210                 215                 220
Glu Ile Leu Glu Ile Lys Gly Gln Asn Trp Glu Glu Gln Val Asn Ser
225                 230                 235                 240
Leu Pro Glu Val Phe Arg Lys Ala Gly Phe Val Ile Glu Ala Phe Thr
                245                 250                 255
Arg Leu Pro Tyr Leu Cys Glu Gly Asp Met Tyr Asn Asp Tyr Tyr Val
            260                 265                 270
Leu Asp Asp Ala Val Phe Val Leu Arg Pro Val
        275                 280
```

<210> 309
<211> 37
<212> PRT
<213> Rat

<400> 309
```
Met Leu Trp Val Leu Leu Ser Leu Thr Pro Leu Leu Ser Pro Leu Ile
 1               5                  10                  15
Phe Phe Pro Val Lys Thr Val Ala Leu Glu Glu Ile Ser Thr Ile Cys
            20                  25                  30
Arg Ala Asp Val Leu
        35
```

<210> 310
<211> 70
<212> PRT
<213> Mouse

<400> 310
Met Ala Ala Ser Trp Gly Gln Val Leu Ala Leu Val Leu Val Ala Ala
1 5 10 15
Leu Trp Gly Gly Thr Gln Pro Leu Leu Lys Arg Ala Ser Ser Gly Leu
20 25 30
Glu Gln Val Arg Glu Arg Thr Trp Ala Trp Gln Leu Leu Gln Glu Ile
35 40 45
Lys Ala Leu Phe Gly Asn Thr Glu Val Arg Leu Ala Leu Thr Asp Glu
50 55 60
Pro Leu Lys Ile Ser Pro
65 70

<210> 311
<211> 58
<212> PRT
<213> Human

<400> 311
Met Leu Leu Ser Ser Leu Val Ser Leu Ala Gly Ser Val Tyr Leu Ala
1 5 10 15
Trp Ile Leu Phe Phe Val Leu Tyr Asp Phe Cys Ile Val Cys Ile Thr
20 25 30
Thr Tyr Ala Ile Asn Val Ser Leu Met Trp Leu Ser Phe Arg Lys Val
35 40 45
Gln Glu Pro Gln Gly Lys Ala Lys Arg His
50 55

<210> 312
<211> 52
<212> PRT
<213> Human

<400> 312
Met Gly Thr Pro Gln Gly Glu Asn Trp Leu Ser Trp Met Phe Glu Lys
1 5 10 15
Leu Val Val Val Met Val Cys Tyr Phe Ile Leu Ser Ile Ile Asn Ser
20 25 30
Met Ala Gln Ser Tyr Ala Lys Arg Ile Gln Gln Arg Leu Asn Ser Glu
35 40 45
Glu Lys Thr Lys
50

<210> 313
<211> 70
<212> PRT
<213> Human

<400> 313
Met Asn Leu Leu Gly Met Ile Phe Ser Met Cys Gly Leu Met Leu Lys
1 5 10 15
Leu Lys Trp Cys Ala Trp Val Ala Val Tyr Cys Ser Phe Ile Ser Phe
20 25 30
Ala Asn Ser Arg Ser Ser Glu Asp Thr Lys Gln Met Met Ser Ser Phe
35 40 45
Met Leu Ser Ile Ser Ala Val Val Met Ser Tyr Leu Gln Asn Pro Gln
50 55 60
Pro Met Thr Pro Pro Trp
65 70

<210> 314
<211> 58

<212> PRT
<213> Mouse

<400> 314
Met Phe Ile Thr Pro Phe Lys Ala Phe Leu Pro Leu Tyr Leu Leu Thr
1   5   10   15
Glu Leu Ser Leu Ile Asp Ile Thr Ser Cys Asp Asp Leu Pro His Ser
            20   25   30
Val Leu Pro Gln His Leu Ser Phe Glu Phe Val Leu Trp Ser Met Tyr
        35   40   45
Leu Leu Ile Cys Cys Phe Val Ile Ile Phe
    50   55

<210> 315
<211> 229
<212> PRT
<213> Rat

<400> 315
Met Ala Ser Ala Leu Glu Glu Leu Gln Lys Asp Leu Glu Glu Val Lys
1   5   10   15
Val Leu Leu Glu Lys Ser Thr Arg Lys Arg Leu Arg Asp Thr Leu Thr
            20   25   30
Asn Glu Lys Ser Lys Ile Glu Thr Glu Leu Arg Asn Lys Met Gln Gln
        35   40   45
Lys Ser Gln Lys Lys Pro Glu Phe Asp Asn Glu Lys Pro Ala Ala Val
    50   55   60
Val Ala Pro Leu Thr Thr Gly Tyr Thr Val Lys Ile Ser Asn Tyr Gly
65   70   75   80
Trp Asp Gln Ser Asp Lys Phe Val Lys Ile Tyr Ile Thr Leu Thr Gly
                85   90   95
Val His Gln Val Pro Ala Glu Asn Val Gln Val His Phe Thr Glu Arg
            100   105   110
Ser Phe Asp Leu Leu Val Lys Asn Leu Asn Gly Lys Asn Tyr Ser Met
        115   120   125
Ile Val Asn Asn Leu Leu Lys Pro Ile Ser Val Glu Ser Ser Ser Lys
    130   135   140
Lys Val Lys Thr Asp Thr Val Ile Ile Leu Cys Arg Lys Lys Ala Glu
145   150   155   160
Asn Thr Arg Trp Asp Tyr Leu Thr Gln Val Glu Lys Glu Cys Lys Glu
                165   170   175
Lys Glu Lys Pro Ser Tyr Asp Thr Glu Ala Asp Pro Ser Glu Gly Leu
            180   185   190
Met Asn Val Leu Lys Lys Ile Tyr Glu Asp Gly Asp Asp Asp Met Lys
        195   200   205
Arg Thr Ile Asn Lys Ala Trp Val Glu Ser Arg Glu Lys Gln Ala Arg
    210   215   220
Glu Asp Thr Glu Phe
225

<210> 316
<211> 128
<212> PRT
<213> Rat

<400> 316
Arg Ala Glu Phe Gly Thr Ser Gly Glu Met Gly Asn Ala Ala Leu Gly
1   5   10   15
Ala Glu Leu Gly Val Arg Val Leu Leu Phe Val Ala Phe Leu Ala Thr
            20   25   30
Glu Leu Leu Pro Pro Phe Gln Arg Arg Ile Gln Pro Glu Glu Leu Trp

```
        35                  40                  45
Leu Tyr Arg Asn Pro Tyr Val Glu Ala Glu Tyr Phe Pro Thr Gly Pro
    50                  55                  60
Met Phe Val Ile Ala Phe Leu Thr Pro Leu Ser Leu Ile Phe Phe Ala
65                  70                  75                  80
Lys Phe Leu Arg Lys Ala Asp Ala Thr Asp Ser Lys Gln Ala Cys Leu
                85                  90                  95
Ala Ala Ser Leu Ala Leu Ala Leu Asn Gly Val Phe Thr Asn Ile Ile
            100                 105                 110
Lys Leu Ile Val Gly Arg Pro Arg Pro Asp Phe Phe Tyr Arg Cys Phe
        115                 120                 125
```

<210> 317
<211> 75
<212> PRT
<213> Rat

<400> 317

```
Ser Ala Gly Val Met Thr Ala Ala Val Phe Phe Gly Cys Ala Phe Ile
 1               5                  10                  15
Ala Phe Gly Pro Ala Leu Ser Leu Tyr Val Phe Thr Ile Ala Thr Asp
            20                  25                  30
Pro Leu Arg Val Ile Phe Leu Ile Ala Gly Ala Phe Phe Trp Leu Val
        35                  40                  45
Ser Leu Leu Leu Ser Ser Val Phe Trp Phe Leu Val Arg Val Ile Thr
    50                  55                  60
Asp Asn Arg Asp Gly Pro Val Gln Asn Tyr Leu
65                  70                  75
```

<210> 318
<211> 43
<212> PRT
<213> Human

<400> 318

```
Met Lys Leu Ser Gly Met Phe Leu Leu Leu Ser Leu Ala Leu Phe Cys
 1               5                  10                  15
Phe Leu Thr Gly Val Phe Ser Gln Gly Gly Gln Val Asp Cys Gly Glu
            20                  25                  30
Ser Arg Thr Pro Arg Pro Thr Ala Leu Gly Asn
        35                  40
```

<210> 319
<211> 86
<212> PRT
<213> Mouse

<400> 319

```
Met Leu Gln Gly Pro Ala Pro Ser Cys Phe Trp Val Phe Ser Gly Ile
 1               5                  10                  15
Cys Val Phe Trp Asp Phe Ile Phe Ile Ile Phe Phe Asn Val Leu Ser
            20                  25                  30
Leu Gly Asn Arg Glu Ile Ser Ala Lys Asp Phe Ala Asp Gln Pro Ala
        35                  40                  45
Gly Ala Gln Gly Met Trp Gly Ile Trp Gly His Thr Ile Thr Cys Gly
    50                  55                  60
Leu Ala Pro Gly Ala Lys Pro Cys Ser Leu Lys Arg Glu Gly Pro Asp
65                  70                  75                  80
Leu Leu Ser Phe Pro Pro
                85
```

<210> 320
<211> 60
<212> PRT
<213> Mouse

<400> 320
Lys Gly Pro Glu Val Ser Cys Cys Ile Lys Tyr Phe Ile Phe Gly Phe
1 5 10 15
Asn Val Ile Phe Trp Phe Leu Gly Ile Thr Phe Leu Gly Ile Gly Leu
20 25 30
Trp Ala Trp Asn Glu Lys Gly Val Leu Ser Asn Ile Ser Ser Ile Thr
35 40 45
Asp Leu Gly Gly Phe Asp Pro Val Trp Leu Phe Leu
50 55 60

<210> 321
<211> 160
<212> PRT
<213> Mouse

<400> 321
Ile Arg His Glu Ala Glu Ala Gly Arg His Gln Pro Glu Gln Leu Ala
1 5 10 15
Ala Asp Ser Arg Thr Glu Thr Val Gly Pro Arg Gln Ser Asn Gly Leu
20 25 30
Thr Gly Pro Gly Leu Pro Thr Trp Gln Leu His Pro Val Leu Phe Pro
35 40 45
Glu Leu Val Leu Trp Val Asn Met Val Pro Cys Phe Leu Leu Ser Leu
50 55 60
Leu Leu Leu Val Arg Pro Ala Pro Val Val Ala Tyr Ser Val Ser Leu
65 70 75 80
Pro Ala Ser Phe Leu Glu Glu Val Ala Gly Ser Gly Glu Ala Glu Gly
85 90 95
Ser Ser Ala Ser Ser Pro Ser Leu Leu Pro Pro Arg Thr Pro Ala Phe
100 105 110
Ser Pro Thr Pro Gly Arg Thr Gln Pro Thr Ala Pro Val Gly Pro Val
115 120 125
Pro Pro Thr Asn Leu Leu Asp Gly Ile Val Asp Phe Phe Arg Gln Tyr
130 135 140
Val Met Leu Ile Ala Val Val Gly Ser Leu Thr Phe Leu Ile Ser Ser
145 150 155 160

<210> 322
<211> 54
<212> PRT
<213> Mouse

<400> 322
Arg Leu Gln Val Asp Thr Ser Gly Ser Lys Val Leu Phe Leu Phe Phe
1 5 10 15
Phe Phe Phe Leu Cys Val Cys Val Leu Val Cys Cys Cys Phe Gly Phe
20 25 30
Pro Gly Thr His Ser Val Asp Gln Ala Ser Pro Lys Leu Arg Asn Leu
35 40 45
Pro Pro Glu Cys Trp Asp
50

<210> 323
<211> 280
<212> PRT
<213> Mouse

<400> 323

```
Leu Asp Ser Arg Ala Cys Arg Ser Thr Leu Val Asp Pro Lys Asn Ser
 1               5                  10                  15
Ala Arg Glu Asn Ile Arg Glu Tyr Val Arg Trp Met Met Tyr Trp Ile
            20                  25                  30
Val Phe Ala Ile Phe Met Ala Ala Glu Thr Phe Thr Asp Ile Phe Ile
        35                  40                  45
Ser Trp Ser Gly Pro Arg Ile Gly Arg Pro Trp Gly Trp Glu Gly Pro
    50                  55                  60
His His His His His Leu Ala Ser Gly Ser His Lys Pro Leu Pro Leu
65                  70                  75                  80
Leu Thr His Arg Phe Pro Phe Tyr Tyr Glu Phe Lys Met Ala Phe Val
                85                  90                  95
Leu Trp Leu Leu Ser Pro Tyr Thr Lys Gly Ala Ser Leu Leu Tyr Arg
            100                 105                 110
Lys Phe Val His Pro Ser Leu Ser Arg His Glu Lys Glu Ile Asp Ala
        115                 120                 125
Cys Ile Val Gln Ala Lys Glu Arg Ser Tyr Glu Thr Met Leu Ser Phe
    130                 135                 140
Gly Lys Arg Ser Leu Asn Ile Ala Ala Ser Ala Ala Val Gln Ala Ala
145                 150                 155                 160
Thr Lys Ser Gln Gly Ala Leu Ala Gly Arg Leu Arg Ser Phe Ser Met
                165                 170                 175
Gln Asp Leu Arg Ser Ile Pro Asp Thr Pro Val Pro Thr Tyr Gln Asp
            180                 185                 190
Pro Leu Tyr Leu Glu Asp Gln Val Pro Arg Arg Arg Pro Pro Ile Gly
        195                 200                 205
Tyr Arg Pro Gly Gly Leu Gln Gly Ser Asp Thr Glu Asp Glu Cys Trp
    210                 215                 220
Ser Asp Asn Glu Ile Val Pro Gln Pro Pro Val Gly Pro Arg Glu Lys
225                 230                 235                 240
Pro Leu Gly Arg Ser Gln Ser Leu Arg Val Val Lys Arg Lys Pro Leu
                245                 250                 255
Thr Arg Glu Gly Thr Ser Arg Ser Leu Lys Val Arg Thr Pro Lys Lys
            260                 265                 270
Ala Met Pro Ser Asp Met Asp Ser
        275                 280
```

<210> 324
<211> 166
<212> PRT
<213> Rat

<400> 324

```
Ala Leu Arg Arg Val Gly Met Glu Leu Pro Ala Val Asn Leu Lys Val
 1               5                  10                  15
Ile Leu Leu Val His Trp Leu Leu Thr Thr Trp Gly Cys Leu Ala Phe
            20                  25                  30
Ser Gly Ser Tyr Ala Trp Gly Asn Phe Thr Ile Leu Ala Leu Gly Val
        35                  40                  45
Trp Ala Val Ala Gln Arg Asp Ser Val Asp Ala Ile Gly Met Phe Leu
    50                  55                  60
Gly Gly Leu Val Ala Thr Ile Phe Leu Asp Ile Ile Tyr Ile Ser Ile
65                  70                  75                  80
Phe Tyr Ser Ser Val Ala Val Gly Asp Thr Gly Arg Phe Ser Ala Gly
                85                  90                  95
Met Ala Ile Phe Ser Leu Leu Leu Lys Pro Phe Ser Cys Cys Leu Val
            100                 105                 110
Tyr His Met His Arg Glu Arg Gly Gly Glu Leu Pro Leu Arg Ser Asp
        115                 120                 125
```

Phe Phe Gly Pro Ser Gln Glu His Ser Ala Tyr Gln Thr Ile Asp Ser
130 135 140
Ser Asp Ser Pro Ala Asp Pro Leu Ala Ser Leu Glu Asn Lys Gly Gln
145 150 155 160
Ala Ala Pro Arg Gly Tyr
165

<210> 325
<211> 338
<212> PRT
<213> Rat

<400> 325
Ile Arg His Glu Ala Glu Ala Gly Arg His Gln Pro Glu Gln Leu Ala
1 5 10 15
Ala Asp Ser Arg Thr Glu Thr Val Gly Pro Arg Gln Ser Asn Gly Leu
20 25 30
Thr Gly Pro Gly Leu Pro Thr Trp Gln Leu His Pro Val Leu Phe Pro
35 40 45
Glu Leu Val Leu Trp Val Asn Met Val Pro Cys Phe Leu Leu Ser Leu
50 55 60
Leu Leu Leu Val Arg Pro Ala Pro Val Val Ala Tyr Ser Val Ser Leu
65 70 75 80
Pro Ala Ser Phe Leu Glu Glu Val Ala Gly Ser Gly Glu Ala Glu Gly
85 90 95
Ser Ser Ala Ser Ser Pro Ser Leu Leu Pro Pro Arg Thr Pro Ala Phe
100 105 110
Ser Pro Thr Pro Gly Arg Thr Gln Pro Thr Ala Pro Val Gly Pro Val
115 120 125
Pro Pro Thr Asn Leu Leu Asp Gly Ile Val Asp Phe Phe Arg Gln Tyr
130 135 140
Val Met Leu Ile Ala Val Val Gly Ser Leu Thr Phe Leu Ile Met Phe
145 150 155 160
Ile Val Cys Ala Ala Leu Ile Thr Arg Gln Lys His Lys Ala Thr Ala
165 170 175
Tyr Tyr Pro Ser Ser Phe Pro Glu Lys Lys Tyr Val Asp Gln Arg Asp
180 185 190
Arg Ala Gly Gly Pro His Ala Phe Ser Glu Val Pro Asp Arg Ala Pro
195 200 205
Asp Ser Arg Gln Glu Glu Gly Leu Asp Ser Ser Gln Gln Leu Gln Ala
210 215 220
Asp Ile Leu Ala Ala Thr Gln Asn Leu Arg Ser Pro Ala Arg Ala Leu
225 230 235 240
Pro Gly Ser Gly Glu Gly Thr Lys Gln Val Lys Gly Gly Ser Glu Glu
245 250 255
Glu Glu Glu Lys Glu Glu Glu Val Phe Ser Gly Gln Glu Glu Pro Arg
260 265 270
Glu Ala Pro Val Cys Gly Val Thr Glu Glu Lys Pro Glu Val Pro Asp
275 280 285
Glu Thr Ala Ser Ala Glu Ala Glu Gly Val Pro Ala Ala Ser Glu Gly
290 295 300
Gln Gly Glu Pro Glu Gly Ser Phe Ser Leu Ala Gln Glu Pro Gln Gly
305 310 315 320
Ala Ala Gly Pro Ser Glu Arg Ser Cys Ala Cys Asn Arg Ile Ser Pro
325 330 335
Asn Val

<210> 326
<211> 347
<212> PRT

<213> Human

<400> 326

```
Ala Trp Ser Arg Pro Arg Tyr Tyr Arg Leu Cys Asp Lys Ala Glu Ala
1               5                   10                  15
Trp Gly Ile Val Leu Glu Thr Val Ala Thr Ala Gly Val Val Thr Ser
            20                  25                  30
Val Ala Phe Met Leu Thr Leu Pro Ile Leu Val Cys Lys Val Gln Asp
        35                  40                  45
Ser Asn Arg Arg Lys Met Leu Pro Thr Gln Phe Leu Phe Leu Leu Gly
    50                  55                  60
Val Leu Gly Ile Phe Gly Leu Thr Phe Ala Phe Ile Ile Gly Leu Asp
65                  70                  75                  80
Gly Ser Thr Gly Pro Thr Arg Phe Phe Leu Phe Gly Ile Leu Phe Ser
                85                  90                  95
Ile Cys Phe Ser Cys Leu Leu Ala His Ala Val Ser Leu Thr Lys Leu
            100                 105                 110
Val Arg Gly Arg Lys Pro Leu Ser Leu Leu Val Ile Leu Gly Leu Ala
        115                 120                 125
Val Gly Phe Ser Leu Val Gln Asp Val Ile Ala Ile Glu Tyr Ile Val
    130                 135                 140
Leu Thr Met Asn Arg Thr Asn Val Asn Val Phe Ser Glu Leu Ser Ala
145                 150                 155                 160
Pro Arg Arg Asn Glu Asp Phe Val Leu Leu Leu Thr Tyr Val Leu Phe
                165                 170                 175
Leu Met Ala Leu Thr Phe Leu Met Ser Ser Phe Thr Phe Cys Gly Ser
            180                 185                 190
Phe Thr Gly Trp Lys Arg His Gly Ala His Ile Tyr Leu Thr Met Leu
        195                 200                 205
Leu Ser Ile Ala Ile Trp Val Ala Trp Ile Thr Leu Leu Met Leu Pro
    210                 215                 220
Asp Phe Asp Arg Arg Trp Asp Asp Thr Ile Leu Ser Ser Ala Leu Ala
225                 230                 235                 240
Ala Asn Gly Trp Val Phe Leu Leu Ala Tyr Val Ser Pro Glu Phe Trp
                245                 250                 255
Leu Leu Thr Lys Gln Arg Asn Pro Met Asp Tyr Pro Val Glu Asp Ala
            260                 265                 270
Phe Cys Lys Pro Gln Leu Val Lys Lys Ser Tyr Gly Val Glu Asn Arg
        275                 280                 285
Ala Tyr Ser Gln Glu Glu Ile Thr Gln Gly Phe Glu Glu Thr Gly Asp
    290                 295                 300
Thr Leu Tyr Ala Pro Tyr Ser Thr His Phe Gln Leu Gln Asn Gln Pro
305                 310                 315                 320
Pro Gln Lys Glu Phe Ser Ile Pro Arg Ala His Ala Trp Pro Ser Pro
                325                 330                 335
Tyr Lys Asp Tyr Glu Val Lys Lys Glu Gly Ser
            340                 345
```

<210> 327
<211> 141
<212> PRT
<213> Human

<400> 327

```
Lys Asn Ser Lys Cys Leu Leu Phe Trp Cys Arg Lys Ile Val Gly Asn
1               5                   10                  15
Arg Gln Glu Pro Met Trp Glu Phe Asn Phe Lys Phe Lys Lys Gln Ser
            20                  25                  30
Pro Arg Leu Lys Ser Lys Cys Thr Gly Gly Leu Gln Pro Pro Val Gln
        35                  40                  45
Tyr Glu Asp Val His Thr Asn Pro Asp Gln Asp Cys Cys Leu Leu Gln
```

50 55 60
Val Thr Thr Leu Asn Phe Ile Phe Ile Pro Ile Val Met Gly Met Ile
65 70 75 80
Phe Thr Leu Phe Thr Ile Asn Val Ser Thr Asp Met Arg His His Arg
85 90 95
Val Arg Leu Val Phe Gln Asp Ser Pro Val His Gly Gly Arg Lys Leu
100 105 110
Arg Ser Glu Gln Gly Val Gln Val Ile Leu Asp Gln Cys Thr Ala Phe
115 120 125
Gly Ser Leu Thr Gly Gly Ile Leu Ser Thr His Ser Pro
130 135 140

<210> 328
<211> 71
<212> PRT
<213> Human

<400> 328
Arg Glu Arg Thr Ser Leu Glu Phe Phe Val Phe Leu Phe Leu Phe Ile
1 5 10 15
Cys Cys Cys Leu His Ser Gly Gly Leu Gly Gly Val Pro Leu Pro Pro
20 25 30
Phe Pro Pro Gln Ala Gln Arg Gly Glu Gly Pro Gly Lys Trp Met Ser
35 40 45
Pro Pro Leu Pro Pro His Pro Val Val Ala Pro Pro Thr Pro Ser Pro
50 55 60
Ser Arg Gly Cys Val Leu Leu
65 70

<210> 329
<211> 109
<212> PRT
<213> Human

<400> 329
Asp Gly Pro Ser Pro Lys Leu Ala Leu Trp Leu Pro Ser Pro Ala Pro
1 5 10 15
Thr Ala Ala Pro Thr Ala Leu Gly Glu Ala Gly Leu Ala Glu His Ser
20 25 30
Gln Arg Asp Asp Arg Trp Leu Leu Val Ala Leu Leu Val Pro Thr Cys
35 40 45
Val Phe Leu Val Val Leu Leu Ala Leu Gly Ile Val Tyr Cys Thr Arg
50 55 60
Cys Gly Pro His Ala Pro Asn Lys Arg Ile Thr Asp Cys Tyr Arg Trp
65 70 75 80
Val Ile His Ala Gly Ser Lys Ser Pro Thr Glu Pro Met Pro Pro Arg
85 90 95
Gly Ser Leu Thr Gly Val Gln Thr Cys Arg Thr Ser Val
100 105

<210> 330
<211> 155
<212> PRT
<213> Human

<400> 330
Ser Val Met Ala Ala Gly Leu Phe Gly Leu Ser Ala Arg Arg Leu Leu
1 5 10 15
Ala Ala Ala Ala Thr Arg Gly Leu Pro Ala Ala Arg Val Arg Trp Glu
20 25 30
Ser Ser Phe Ser Arg Thr Val Val Ala Pro Ser Ala Val Ala Gly Lys

```
        35                  40                  45
Arg Pro Pro Glu Pro Thr Thr Pro Trp Gln Glu Asp Pro Glu Pro Glu
    50                  55                  60
Asp Glu Asn Leu Tyr Glu Lys Asn Pro Asp Ser His Gly Tyr Asp Lys
65                  70                  75                  80
Asp Pro Val Leu Asp Val Trp Asn Met Arg Leu Val Phe Phe Phe Gly
                85                  90                  95
Val Ser Ile Ile Leu Val Leu Gly Ser Thr Phe Val Ala Tyr Leu Pro
            100                 105                 110
Asp Tyr Arg Met Lys Glu Trp Ser Arg Arg Glu Ala Glu Arg Leu Val
        115                 120                 125
Lys Tyr Arg Glu Ala Asn Gly Leu Pro Ile Met Glu Ser Asn Cys Phe
    130                 135                 140
Asp Pro Ser Lys Ile Gln Leu Pro Glu Asp Glu
145                 150                 155

      <210> 331
      <211> 299
      <212> PRT
      <213> Human

      <400> 331
Met Gly Thr Lys Ala Gln Val Glu Arg Lys Leu Leu Cys Leu Phe Ile
 1               5                  10                  15
Leu Ala Ile Leu Leu Cys Ser Leu Ala Leu Gly Ser Val Thr Val His
            20                  25                  30
Ser Ser Glu Pro Glu Val Arg Ile Pro Glu Asn Asn Pro Val Lys Leu
        35                  40                  45
Ser Cys Ala Tyr Ser Gly Phe Ser Ser Pro Arg Val Glu Trp Lys Phe
    50                  55                  60
Asp Gln Gly Asp Thr Thr Arg Leu Val Cys Tyr Asn Asn Lys Ile Thr
65                  70                  75                  80
Ala Ser Tyr Glu Asp Arg Val Thr Phe Leu Pro Thr Gly Ile Thr Phe
                85                  90                  95
Lys Ser Val Thr Arg Glu Asp Thr Gly Thr Tyr Thr Cys Met Val Ser
            100                 105                 110
Glu Glu Gly Gly Asn Ser Tyr Gly Glu Val Lys Val Lys Leu Ile Val
        115                 120                 125
Leu Val Pro Pro Ser Lys Pro Thr Val Asn Ile Pro Ser Ser Ala Thr
    130                 135                 140
Ile Gly Asn Arg Ala Val Leu Thr Cys Ser Glu Gln Asp Gly Ser Pro
145                 150                 155                 160
Pro Ser Glu Tyr Thr Trp Phe Lys Asp Gly Ile Val Met Pro Thr Asn
                165                 170                 175
Pro Lys Ser Thr Arg Ala Phe Ser Asn Ser Ser Tyr Val Leu Asn Pro
            180                 185                 190
Thr Thr Gly Glu Leu Val Phe Asp Pro Leu Ser Ala Ser Asp Thr Gly
        195                 200                 205
Glu Tyr Ser Cys Glu Ala Arg Asn Gly Tyr Gly Thr Pro Met Thr Ser
    210                 215                 220
Asn Ala Val Arg Met Glu Ala Val Glu Arg Asn Val Gly Val Ile Val
225                 230                 235                 240
Ala Ala Val Leu Val Thr Leu Ile Leu Leu Gly Ile Leu Val Phe Gly
                245                 250                 255
Ile Trp Phe Ala Tyr Ser Arg Gly His Phe Asp Arg Thr Lys Lys Gly
            260                 265                 270
Thr Ser Ser Lys Lys Val Ile Tyr Ser Gln Pro Ser Ala Arg Ser Glu
        275                 280                 285
Gly Glu Phe Lys Gln Thr Ser Ser Phe Leu Val
    290                 295
```

<210> 332
<211> 299
<212> PRT
<213> Mouse

<400> 332
Ala Arg Ala Gly Ala Cys Tyr Cys Pro Ala Gly Phe Leu Gly Ala Asp
1 5 10 15
Cys Ser Leu Ala Cys Pro Gln Gly Arg Phe Gly Pro Ser Cys Ala His
20 25 30
Val Cys Thr Cys Gly Gln Gly Ala Ala Cys Asp Pro Val Ser Gly Thr
35 40 45
Cys Ile Cys Pro Pro Gly Lys Thr Gly Gly His Cys Glu Arg Gly Cys
50 55 60
Pro Gln Asp Arg Phe Gly Lys Gly Cys Glu His Lys Cys Ala Cys Arg
65 70 75 80
Asn Gly Gly Leu Cys His Ala Thr Asn Gly Ser Cys Ser Cys Pro Leu
85 90 95
Gly Trp Met Gly Pro His Cys Glu His Ala Cys Pro Ala Gly Arg Tyr
100 105 110
Gly Ala Ala Cys Leu Leu Glu Cys Ser Cys Gln Asn Asn Gly Ser Cys
115 120 125
Glu Pro Thr Ser Gly Ala Cys Leu Cys Gly Pro Gly Phe Tyr Gly Gln
130 135 140
Ala Cys Glu Asp Thr Cys Pro Ala Gly Phe His Gly Ser Gly Cys Gln
145 150 155 160
Arg Val Cys Glu Cys Gln Gln Gly Ala Pro Cys Asp Pro Val Ser Gly
165 170 175
Arg Cys Leu Cys Pro Ala Gly Phe Arg Gly Gln Phe Cys Glu Arg Gly
180 185 190
Cys Lys Pro Gly Phe Phe Gly Asp Gly Cys Leu Gln Gln Cys Asn Cys
195 200 205
Pro Thr Gly Val Pro Cys Asp Pro Ile Ser Gly Leu Cys Leu Cys Pro
210 215 220
Pro Gly Arg Ala Gly Thr Thr Cys Asp Leu Asp Cys Arg Arg Gly Arg
225 230 235 240
Phe Gly Pro Gly Cys Ala Leu Arg Cys Asp Cys Gly Gly Gly Ala Asp
245 250 255
Cys Asp Pro Ile Ser Gly Gln Cys His Cys Val Asp Ser Tyr Thr Gly
260 265 270
Pro Thr Cys Arg Glu Val Pro Thr Gln Leu Ser Ser Ile Arg Pro Ala
275 280 285
Pro Gln His Ser Ser Ser Lys Ala Met Lys His
290 295

<210> 333
<211> 109
<212> PRT
<213> Mouse

<400> 333
Gly Thr Arg Val Gly Thr Pro Tyr Tyr Met Ser Pro Glu Arg Ile His
1 5 10 15
Glu Asn Gly Tyr Asn Phe Lys Ser Asp Ile Trp Ser Leu Gly Cys Leu
20 25 30
Leu Tyr Glu Met Ala Ala Leu Gln Ser Pro Phe Tyr Gly Asp Lys Met
35 40 45
Asn Leu Tyr Ser Leu Cys Lys Lys Ile Glu Gln Cys Asp Tyr Pro Pro
50 55 60
Leu Pro Ser Asp His Tyr Ser Glu Glu Leu Arg Gln Leu Val Asn Ile
65 70 75 80

Cys Ile Asn Pro Asp Pro Glu Lys Arg Pro Asp Ile Ala Tyr Val Tyr
85 90 95
Asp Val Ala Lys Arg Met His Ala Cys Thr Ala Ser Thr
100 105

<210> 334
<211> 787
<212> PRT
<213> Mouse

<400> 334
Lys Val Glu Gly Glu Gly Arg Gly Arg Trp Ala Leu Gly Leu Leu Arg
1 5 10 15
Thr Phe Asp Ala Gly Glu Phe Ala Gly Trp Glu Lys Val Gly Ser Gly
20 25 30
Gly Phe Gly Gln Val Tyr Lys Val Arg His Val His Trp Lys Thr Trp
35 40 45
Leu Ala Ile Lys Cys Ser Pro Ser Leu His Val Asp Asp Arg Glu Arg
50 55 60
Met Glu Leu Leu Glu Glu Ala Lys Lys Met Glu Met Ala Lys Phe Arg
65 70 75 80
Tyr Ile Leu Pro Val Tyr Gly Ile Cys Gln Glu Pro Val Gly Leu Val
85 90 95
Met Glu Tyr Met Glu Thr Gly Ser Leu Glu Lys Leu Leu Ala Ser Glu
100 105 110
Pro Leu Pro Trp Asp Leu Arg Phe Arg Ile Val His Glu Thr Ala Val
115 120 125
Gly Met Asn Phe Leu His Cys Met Ser Pro Pro Leu Leu His Leu Asp
130 135 140
Leu Lys Pro Ala Asn Ile Leu Leu Asp Ala His Tyr His Val Lys Ile
145 150 155 160
Ser Asp Phe Gly Leu Ala Lys Cys Asn Gly Met Ser His Ser His Asp
165 170 175
Leu Ser Met Asp Gly Leu Phe Gly Thr Ile Ala Tyr Leu Pro Pro Glu
180 185 190
Arg Ile Arg Glu Lys Ser Arg Leu Phe Asp Thr Lys His Asp Val Tyr
195 200 205
Ser Phe Ala Ile Val Ile Trp Gly Val Leu Thr Gln Lys Lys Pro Phe
210 215 220
Ala Asp Glu Lys Asn Ile Leu His Ile Met Met Lys Val Val Lys Gly
225 230 235 240
His Arg Pro Glu Leu Pro Pro Ile Cys Arg Pro Arg Pro Arg Ala Cys
245 250 255
Ala Ser Leu Ile Gly Leu Met Gln Arg Cys Trp His Ala Asp Pro Gln
260 265 270
Val Arg Pro Thr Phe Gln Glu Ile Thr Ser Glu Thr Glu Asp Leu Cys
275 280 285
Glu Lys Pro Asp Glu Glu Val Lys Asp Leu Ala His Glu Pro Gly Glu
290 295 300
Lys Ser Ser Leu Glu Ser Lys Ser Glu Ala Arg Pro Glu Ser Ser Arg
305 310 315 320
Leu Lys Arg Ala Ser Ala Pro Pro Phe Asp Asn Asp Cys Ser Leu Ser
325 330 335
Glu Leu Leu Ser Gln Leu Asp Ser Gly Ile Ser Gln Thr Leu Glu Gly
340 345 350
Pro Glu Glu Leu Ser Arg Ser Ser Ser Glu Cys Lys Leu Pro Ser Ser
355 360 365
Ser Ser Gly Lys Arg Leu Ser Gly Val Ser Ser Val Asp Ser Ala Phe
370 375 380
Ser Ser Arg Gly Ser Leu Ser Leu Ser Phe Glu Arg Glu Ala Ser Thr
385 390 395 400

```
Gly Asp Leu Gly Pro Thr Asp Ile Gln Lys Lys Lys Leu Val Asp Ala
                405                 410                 415
Ile Ile Ser Gly Asp Thr Ser Arg Leu Met Lys Ile Leu Gln Pro Gln
            420                 425                 430
Asp Val Asp Leu Val Leu Asp Ser Ser Ala Ser Leu Leu His Leu Ala
        435                 440                 445
Val Glu Ala Gly Gln Glu Glu Cys Val Lys Trp Leu Leu Leu Asn Asn
    450                 455                 460
Ala Asn Pro Asn Leu Thr Asn Arg Lys Gly Ser Thr Pro Leu His Met
465                 470                 475                 480
Ala Val Glu Arg Lys Gly Arg Gly Ile Val Glu Leu Leu Leu Ala Arg
                485                 490                 495
Lys Thr Ser Val Asn Ala Lys Asp Glu Asp Gln Trp Thr Ala Leu His
            500                 505                 510
Phe Ala Ala Gln Asn Gly Asp Glu Ala Ser Thr Arg Leu Leu Leu Glu
        515                 520                 525
Lys Asn Ala Ser Val Asn Glu Val Asp Phe Glu Gly Arg Thr Pro Met
    530                 535                 540
His Val Ala Cys Gln His Gly Gln Glu Asn Ile Val Arg Thr Leu Leu
545                 550                 555                 560
Arg Arg Gly Val Asp Val Gly Leu Gln Gly Lys Asp Ala Trp Leu Pro
                565                 570                 575
Leu His Tyr Ala Ala Trp Gln Gly His Leu Pro Ile Val Lys Leu Leu
            580                 585                 590
Ala Lys Gln Pro Gly Val Ser Val Asn Ala Gln Thr Leu Asp Gly Arg
        595                 600                 605
Thr Pro Leu His Leu Ala Ala Gln Arg Gly His Tyr Arg Val Ala Arg
    610                 615                 620
Ile Leu Ile Asp Leu Cys Ser Asp Val Asn Ile Cys Ser Leu Gln Ala
625                 630                 635                 640
Gln Thr Pro Leu His Val Ala Ala Glu Thr Gly His Thr Ser Thr Ala
                645                 650                 655
Arg Leu Leu Leu His Arg Gly Ala Gly Lys Glu Ala Leu Thr Ser Glu
            660                 665                 670
Gly Tyr Thr Ala Leu His Leu Ala Ala Gln Asn Gly His Leu Ala Thr
        675                 680                 685
Val Lys Leu Leu Ile Glu Glu Lys Ala Asp Val Met Ala Arg Gly Pro
    690                 695                 700
Leu Asn Gln Thr Ala Leu His Leu Ala Ala Ala Arg Gly His Ser Glu
705                 710                 715                 720
Val Val Glu Glu Leu Val Ser Ala Asp Leu Ile Asp Leu Ser Asp Glu
                725                 730                 735
Gln Gly Leu Ser Ala Leu His Leu Ala Ala Gln Gly Arg His Ser Gln
            740                 745                 750
Thr Val Glu Thr Leu Leu Lys His Gly Ala His Ile Asn Leu Gln Ser
        755                 760                 765
Leu Lys Phe Gln Gly Gly Gln Ser Ser Ala Ala Thr Leu Leu Arg Arg
    770                 775                 780
Ser Lys Thr
785

&lt;210&gt; 335
&lt;211&gt; 194
&lt;212&gt; PRT
&lt;213&gt; Mouse

&lt;400&gt; 335
Pro Gly Cys Lys Ser Cys Thr Val Cys Arg His Gly Leu Cys Arg Ser
 1               5                  10                  15
Val Glu Lys Asp Ser Val Val Cys Glu Cys His Pro Gly Trp Thr Gly
            20                  25                  30
```

```
Pro Leu Cys Asp Gln Glu Ala Arg Asp Pro Cys Leu Gly His Ser Cys
        35                  40                  45
Arg His Gly Thr Cys Met Ala Thr Gly Asp Ser Tyr Val Cys Lys Cys
    50                  55                  60
Ala Glu Gly Tyr Gly Gly Ala Leu Cys Asp Gln Lys Asn Asp Ser Ala
65                  70                  75                  80
Ser Ala Cys Ser Ala Phe Lys Cys His His Gly Gln Cys His Ile Ser
                85                  90                  95
Asp Arg Gly Glu Pro Tyr Cys Leu Cys Gln Pro Gly Phe Ser Gly His
            100                 105                 110
His Cys Glu Gln Glu Asn Pro Cys Met Gly Glu Ile Val Arg Glu Ala
        115                 120                 125
Ile Arg Arg Gln Lys Asp Tyr Ala Ser Cys Ala Thr Ala Ser Lys Val
    130                 135                 140
Pro Ile Met Glu Cys Arg Gly Gly Cys Gly Thr Thr Cys Cys Gln Pro
145                 150                 155                 160
Ile Arg Ser Lys Arg Arg Lys Tyr Val Phe Gln Cys Thr Asp Gly Ser
                165                 170                 175
Ser Phe Val Glu Glu Val Glu Arg His Leu Glu Cys Gly Cys Arg Ala
            180                 185                 190
Cys Ser


      <210> 336
      <211> 274
      <212> PRT
      <213> Human

      <400> 336
Tyr Arg Tyr Cys Gln His Arg Cys Val Asn Leu Pro Gly Ser Phe Arg
 1               5                  10                  15
Cys Gln Cys Glu Pro Gly Phe Gln Leu Gly Pro Asn Asn Arg Ser Cys
            20                  25                  30
Val Asp Val Asn Glu Cys Asp Met Gly Ala Pro Cys Glu Gln Arg Cys
        35                  40                  45
Phe Asn Ser Tyr Gly Thr Phe Leu Cys Arg Cys His Gln Gly Tyr Glu
    50                  55                  60
Leu His Arg Asp Gly Phe Ser Cys Ser Asp Ile Asp Glu Cys Ser Tyr
65                  70                  75                  80
Ser Ser Tyr Leu Cys Gln Tyr Arg Cys Val Asn Glu Pro Gly Arg Phe
                85                  90                  95
Ser Cys His Cys Pro Gln Gly Tyr Gln Leu Leu Ala Thr Arg Leu Cys
            100                 105                 110
Gln Asp Ile Asp Glu Cys Glu Ser Gly Ala His Gln Cys Ser Glu Ala
        115                 120                 125
Gln Thr Cys Val Asn Phe His Gly Gly Tyr Arg Cys Val Asp Thr Asn
    130                 135                 140
Arg Cys Val Glu Pro Tyr Ile Gln Val Ser Glu Asn Arg Cys Leu Cys
145                 150                 155                 160
Pro Ala Ser Asn Pro Leu Cys Arg Glu Gln Pro Ser Ser Ile Val His
                165                 170                 175
Arg Tyr Met Thr Ile Thr Ser Glu Arg Ser Val Pro Ala Asp Val Phe
            180                 185                 190
Gln Ile Gln Ala Thr Ser Val Tyr Pro Gly Ala Tyr Asn Ala Phe Gln
        195                 200                 205
Ile Arg Ala Gly Asn Ser Gln Gly Asp Phe Tyr Ile Arg Gln Ile Asn
    210                 215                 220
Asn Val Ser Ala Met Leu Val Leu Ala Arg Pro Val Thr Gly Pro Arg
225                 230                 235                 240
Glu Tyr Val Leu Asp Leu Glu Met Val Thr Met Asn Ser Leu Met Ser
                245                 250                 255
```

Tyr Arg Ala Ser Ser Val Leu Arg Leu Thr Val Phe Val Gly Ala Tyr
260 265 270
Thr Phe

<210> 337
<211> 316
<212> PRT
<213> Mouse

<400> 337
His Glu Glu Glu Pro Cys Asn Asn Gly Ser Glu Ile Leu Ala Tyr Asn
1 5 10 15
Ile Asp Leu Gly Asp Ser Cys Ile Thr Val Gly Asn Thr Thr Thr His
20 25 30
Val Met Lys Asn Leu Leu Pro Glu Thr Thr Tyr Arg Ile Arg Ile Gln
35 40 45
Ala Ile Asn Glu Ile Gly Val Gly Pro Phe Ser Gln Phe Ile Lys Ala
50 55 60
Lys Thr Arg Pro Leu Pro Pro Ser Pro Pro Arg Leu Glu Cys Ala Ala
65 70 75 80
Ser Gly Pro Gln Ser Leu Lys Leu Lys Trp Gly Asp Ser Asn Ser Lys
85 90 95
Thr His Ala Ala Gly Asp Met Val Tyr Thr Leu Gln Leu Glu Asp Arg
100 105 110
Asn Lys Arg Phe Ile Ser Ile Tyr Arg Gly Pro Ser His Thr Tyr Lys
115 120 125
Val Gln Arg Leu Thr Glu Phe Thr Cys Tyr Ser Phe Arg Ile Gln Ala
130 135 140
Met Ser Glu Ala Gly Glu Gly Pro Tyr Ser Glu Thr Tyr Thr Phe Ser
145 150 155 160
Thr Thr Lys Ser Val Pro Pro Thr Leu Lys Ala Pro Arg Val Thr Gln
165 170 175
Leu Glu Gly Asn Ser Cys Glu Ile Phe Trp Glu Thr Val Pro Pro Met
180 185 190
Arg Gly Asp Pro Val Ser Tyr Val Leu Gln Val Leu Val Gly Arg Asp
195 200 205
Ser Glu Tyr Lys Gln Val Tyr Lys Gly Glu Glu Ala Thr Phe Gln Ile
210 215 220
Ser Gly Leu Gln Ser Asn Thr Asp Tyr Arg Phe Arg Val Cys Ala Cys
225 230 235 240
Arg Arg Cys Val Asp Thr Ser Gln Glu Leu Ser Gly Ala Phe Ser Pro
245 250 255
Ser Ala Ala Phe Met Leu Gln Gln Arg Glu Val Met Leu Thr Gly Asp
260 265 270
Leu Gly Gly Met Glu Glu Ala Lys Met Lys Gly Met Met Pro Thr Asp
275 280 285
Glu Gln Phe Ala Ala Leu Ile Val Leu Gly Phe Ala Thr Leu Ser Ile
290 295 300
Leu Phe Ala Phe Ile Leu Gln Tyr Phe Leu Met Lys
305 310 315

<210> 338
<211> 237
<212> PRT
<213> Mouse

<400> 338
Met Leu Ser Leu Arg Ser Leu Leu Pro His Leu Gly Leu Phe Leu Cys
1 5 10 15
Leu Ala Leu His Leu Ser Pro Ser Leu Ser Ala Ser Asp Asn Gly Ser

```
                20                      25                      30
Cys Val Val Leu Asp Asn Ile Tyr Thr Ser Asp Ile Leu Glu Ile Ser
            35                      40                      45
Thr Met Ala Asn Val Ser Gly Gly Asp Val Thr Tyr Thr Val Thr Val
        50                      55                      60
Pro Val Asn Asp Ser Val Ser Ala Val Ile Leu Lys Ala Val Lys Glu
65                      70                      75                      80
Asp Asp Ser Pro Val Gly Thr Trp Ser Gly Thr Tyr Glu Lys Cys Asn
                    85                      90                      95
Asp Ser Ser Val Tyr Tyr Asn Leu Thr Ser Gln Ser Gln Ser Val Phe
                100                     105                     110
Gln Thr Asn Trp Thr Val Pro Thr Ser Glu Asp Val Thr Lys Val Asn
            115                     120                     125
Leu Gln Val Leu Ile Val Val Asn Arg Thr Ala Ser Lys Ser Ser Val
        130                     135                     140
Lys Met Glu Gln Val Gln Pro Ser Ala Ser Thr Pro Ile Pro Glu Ser
145                     150                     155                     160
Ser Glu Thr Ser Gln Thr Ile Asn Thr Thr Pro Thr Val Asn Thr Ala
                    165                     170                     175
Lys Thr Thr Ala Lys Asp Thr Ala Asn Thr Thr Ala Val Thr Thr Ala
                180                     185                     190
Asn Thr Thr Ala Asn Thr Thr Ala Val Thr Thr Ala Lys Thr Thr Ala
            195                     200                     205
Lys Ser Leu Ala Ile Arg Thr Leu Gly Ser Pro Leu Ala Gly Ala Leu
        210                     215                     220
His Ile Leu Leu Val Phe Leu Ile Ser Lys Leu Leu Phe
225                     230                     235
```

<210> 339
<211> 469
<212> PRT
<213> Mouse

<400> 339

```
Met Leu Cys Leu Cys Leu Tyr Val Pro Ile Ala Gly Ala Ala Gln Thr
 1               5                  10                  15
Glu Phe Gln Tyr Phe Glu Ser Lys Gly Leu Pro Ala Glu Leu Lys Ser
                20                      25                      30
Ile Phe Lys Leu Ser Val Phe Ile Pro Ser Gln Glu Phe Ser Thr Tyr
            35                      40                      45
Arg Gln Trp Lys Gln Lys Ile Val Gln Ala Gly Asp Lys Asp Leu Asp
        50                      55                      60
Gly Gln Leu Asp Phe Glu Glu Phe Val His Tyr Leu Gln Asp His Glu
65                      70                      75                      80
Lys Lys Leu Arg Leu Val Phe Lys Ser Leu Asp Lys Lys Asn Asp Gly
                    85                      90                      95
Arg Ile Asp Ala Gln Glu Ile Met Gln Ser Leu Arg Asp Leu Gly Val
                100                     105                     110
Lys Ile Ser Glu Gln Gln Ala Glu Lys Ile Leu Lys Ser Met Asp Lys
            115                     120                     125
Asn Gly Thr Met Thr Ile Asp Trp Asn Glu Trp Arg Asp Tyr His Leu
        130                     135                     140
Leu His Pro Val Glu Asn Ile Pro Glu Ile Ile Leu Tyr Trp Lys His
145                     150                     155                     160
Ser Thr Ile Phe Asp Val Gly Glu Asn Leu Thr Val Pro Asp Glu Phe
                    165                     170                     175
Thr Val Glu Glu Arg Gln Thr Gly Met Trp Trp Arg His Leu Val Ala
                180                     185                     190
Gly Gly Gly Ala Gly Ala Val Ser Arg Thr Cys Thr Ala Pro Leu Asp
            195                     200                     205
Arg Leu Lys Val Leu Met Gln Val His Ala Ser Arg Ser Asn Asn Met
```

```
    210                 215                 220
Cys Ile Val Gly Gly Phe Thr Gln Met Ile Arg Glu Gly Gly Ala Lys
225                 230                 235                 240
Ser Leu Trp Arg Gly Asn Gly Ile Asn Val Leu Lys Ile Ala Pro Glu
                245                 250                 255
Ser Ala Ile Lys Phe Met Ala Tyr Glu Gln Met Lys Arg Leu Val Gly
            260                 265                 270
Ser Asp Gln Glu Thr Leu Arg Ile His Glu Arg Leu Val Ala Gly Ser
        275                 280                 285
Leu Ala Gly Ala Ile Ala Gln Ser Ser Ile Tyr Pro Met Glu Val Leu
    290                 295                 300
Lys Thr Arg Met Ala Leu Arg Lys Thr Gly Gln Tyr Ser Gly Met Leu
305                 310                 315                 320
Asp Cys Ala Arg Arg Ile Leu Ala Lys Glu Gly Val Ala Ala Phe Tyr
                325                 330                 335
Lys Gly Tyr Ile Pro Asn Met Leu Gly Ile Ile Pro Tyr Ala Gly Ile
            340                 345                 350
Asp Leu Ala Val Tyr Glu Thr Leu Lys Asn Thr Trp Leu Gln Arg Tyr
        355                 360                 365
Ala Val Asn Ser Ala Asp Pro Gly Val Phe Val Leu Leu Ala Cys Gly
    370                 375                 380
Thr Ile Ser Ser Thr Cys Gly Gln Leu Ala Ser Tyr Pro Leu Ala Leu
385                 390                 395                 400
Val Arg Thr Arg Met Gln Ala Gln Ala Ser Ile Glu Gly Ala Pro Glu
                405                 410                 415
Val Thr Met Ser Ser Leu Phe Lys Gln Ile Leu Arg Thr Glu Gly Ala
            420                 425                 430
Phe Gly Leu Tyr Arg Gly Leu Ala Pro Asn Phe Met Lys Val Ile Pro
        435                 440                 445
Ala Val Ser Ile Ser Tyr Val Val Tyr Glu Asn Leu Lys Ile Thr Leu
    450                 455                 460
Gly Val Gln Ser Arg
465

      <210> 340
      <211> 99
      <212> PRT
      <213> Mouse

      <400> 340
Met Arg Leu Leu Ala Ala Ala Leu Leu Leu Leu Leu Leu Ala Leu Cys
 1               5                  10                  15
Ala Ser Arg Val Asp Gly Ser Lys Cys Lys Cys Ser Arg Lys Gly Pro
            20                  25                  30
Lys Ile Arg Tyr Ser Asp Val Lys Lys Leu Glu Met Lys Pro Lys Tyr
        35                  40                  45
Pro His Cys Glu Glu Lys Met Val Ile Val Thr Thr Lys Ser Met Ser
    50                  55                  60
Arg Tyr Arg Gly Gln Glu His Cys Leu His Pro Lys Leu Gln Ser Thr
65                  70                  75                  80
Lys Arg Phe Ile Lys Trp Tyr Asn Ala Trp Asn Glu Lys Arg Arg Val
                85                  90                  95
Tyr Glu Glu


      <210> 341
      <211> 431
      <212> PRT
      <213> Mouse

      <400> 341
```

Met Asp Ala Arg Trp Trp Ala Val Val Val Leu Ala Thr Leu Pro Ser
1 5 10 15
Leu Gly Ala Gly Gly Glu Ser Pro Glu Ala Pro Pro Gln Ser Trp Thr
20 25 30
Gln Leu Trp Leu Phe Arg Phe Leu Leu Asn Val Ala Gly Tyr Ala Ser
35 40 45
Phe Met Val Pro Gly Tyr Leu Leu Val Gln Tyr Leu Arg Arg Lys Asn
50 55 60
Tyr Leu Glu Thr Gly Arg Gly Leu Cys Phe Pro Leu Val Lys Ala Cys
65 70 75 80
Val Phe Gly Asn Glu Pro Lys Ala Pro Asp Glu Val Leu Leu Ala Pro
85 90 95
Arg Thr Glu Thr Ala Glu Ser Thr Pro Ser Trp Gln Val Leu Lys Leu
100 105 110
Val Phe Cys Ala Ser Gly Leu Gln Val Ser Tyr Leu Thr Trp Gly Ile
115 120 125
Leu Gln Glu Arg Val Met Thr Gly Ser Tyr Gly Ala Thr Ala Thr Ser
130 135 140
Pro Gly Glu His Phe Thr Asp Ser Gln Phe Leu Val Leu Met Asn Arg
145 150 155 160
Val Leu Ala Leu Val Val Ala Gly Leu Tyr Cys Val Leu Arg Lys Gln
165 170 175
Pro Arg His Gly Ala Pro Met Tyr Arg Tyr Ser Phe Ala Ser Leu Ser
180 185 190
Asn Val Leu Ser Ser Trp Cys Gln Tyr Glu Ala Leu Lys Phe Val Ser
195 200 205
Phe Pro Thr Gln Val Leu Ala Lys Ala Ser Lys Val Ile Pro Val Met
210 215 220
Met Met Gly Lys Leu Val Ser Arg Arg Ser Tyr Glu His Trp Glu Tyr
225 230 235 240
Leu Thr Ala Gly Leu Ile Ser Ile Gly Val Ser Met Phe Leu Leu Ser
245 250 255
Ser Gly Pro Glu Pro Arg Ser Ser Pro Ala Thr Thr Leu Ser Gly Leu
260 265 270
Val Leu Leu Ala Gly Tyr Ile Ala Phe Asp Ser Phe Thr Ser Asn Trp
275 280 285
Gln Asp Ala Leu Phe Ala Tyr Lys Met Ser Ser Val Gln Met Met Phe
290 295 300
Gly Val Asn Leu Phe Ser Cys Leu Phe Thr Val Gly Ser Leu Leu Glu
305 310 315 320
Gln Gly Ala Leu Leu Glu Gly Ala Arg Phe Met Gly Arg His Ser Glu
325 330 335
Phe Ala Leu His Ala Leu Leu Leu Ser Ile Cys Ser Ala Phe Gly Gln
340 345 350
Leu Phe Ile Phe Tyr Thr Ile Gly Gln Phe Gly Ala Ala Val Phe Thr
355 360 365
Ile Ile Met Thr Leu Arg Gln Ala Ile Ala Ile Leu Leu Ser Cys Leu
370 375 380
Leu Tyr Gly His Thr Val Thr Val Val Gly Gly Leu Gly Val Ala Val
385 390 395 400
Val Phe Thr Ala Leu Leu Leu Arg Val Tyr Ala Arg Gly Arg Lys Gln
405 410 415
Arg Gly Lys Lys Ala Val Pro Thr Glu Pro Pro Val Gln Lys Val
420 425 430

<210> 342
<211> 51
<212> PRT
<213> Mouse

<400> 342

Leu Lys Phe Ser His Pro Cys Leu Glu Asp His Asn Ser Tyr Cys Ile
1 5 10 15
Asn Gly Ala Cys Ala Phe His His Glu Leu Lys Gln Ala Ile Cys Arg
20 25 30
Cys Phe Thr Gly Tyr Thr Gly Gln Arg Cys Glu His Leu Thr Leu Thr
35 40 45
Ser Tyr Ala
50

<210> 343
<211> 51
<212> PRT
<213> Human
<400> 343
Leu Lys Phe Ser His Leu Cys Leu Glu Asp His Asn Ser Tyr Cys Ile
1 5 10 15
Asn Gly Ala Cys Ala Phe His His Glu Leu Glu Lys Ala Ile Cys Arg
20 25 30
Cys Phe Thr Gly Tyr Thr Gly Glu Arg Cys Glu His Leu Thr Leu Thr
35 40 45
Ser Tyr Ala
50

<210> 344
<211> 95
<212> PRT
<213> Human

<400> 344
Ala Ala Ala Leu Leu Leu Leu Leu Leu Ala Leu Tyr Thr Ala Arg Val
1 5 10 15
Asp Gly Ser Lys Cys Lys Cys Ser Arg Lys Gly Pro Lys Ile Arg Tyr
20 25 30
Ser Asp Val Lys Lys Leu Glu Met Lys Pro Lys Tyr Pro His Cys Glu
35 40 45
Glu Lys Met Val Ile Ile Thr Thr Lys Ser Val Ser Arg Tyr Arg Gly
50 55 60
Gln Glu His Cys Leu His Pro Lys Leu Gln Ser Thr Lys Arg Phe Ile
65 70 75 80
Lys Trp Tyr Asn Ala Trp Asn Glu Lys Arg Arg Val Tyr Glu Glu
85 90 95

<210> 345
<211> 77
<212> PRT
<213> Mouse

<400> 345
Ser Lys Cys Lys Cys Ser Arg Lys Gly Pro Lys Ile Arg Tyr Ser Asp
1 5 10 15
Val Lys Lys Leu Glu Met Lys Pro Lys Tyr Pro His Cys Glu Glu Lys
20 25 30
Met Val Ile Val Thr Thr Lys Ser Met Ser Arg Tyr Arg Gly Gln Glu
35 40 45
His Cys Leu His Pro Lys Leu Gln Ser Thr Lys Arg Phe Ile Lys Trp
50 55 60
Tyr Asn Ala Trp Asn Glu Lys Arg Arg Val Tyr Glu Glu
65 70 75

<210> 346
<211> 77

<212> PRT
<213> Human

<400> 346
Ser Lys Cys Lys Cys Ser Arg Lys Gly Pro Lys Ile Arg Tyr Ser Asp
1 5 10 15
Val Lys Lys Leu Glu Met Lys Pro Lys Tyr Pro His Cys Glu Glu Lys
20 25 30
Met Val Ile Ile Thr Thr Lys Ser Val Ser Arg Tyr Arg Gly Gln Glu
35 40 45
His Cys Leu His Pro Lys Leu Gln Ser Thr Lys Arg Phe Ile Lys Trp
50 55 60
Tyr Asn Ala Trp Asn Glu Lys Arg Arg Val Tyr Glu Glu
65 70 75

<210> 347
<211> 215
<212> PRT
<213> Mouse

<400> 347
Met Leu Ser Leu Arg Ser Leu Leu Pro His Leu Gly Leu Phe Leu Cys
1 5 10 15
Leu Ala Leu His Leu Ser Pro Ser Leu Ser Ala Ser Asp Asn Gly Ser
20 25 30
Cys Val Val Leu Asp Asn Ile Tyr Thr Ser Asp Ile Leu Glu Ile Ser
35 40 45
Thr Met Ala Asn Val Ser Gly Gly Asp Val Thr Tyr Thr Val Thr Val
50 55 60
Pro Val Asn Asp Ser Val Ser Ala Val Ile Leu Lys Ala Val Lys Glu
65 70 75 80
Asp Asp Ser Pro Val Gly Thr Trp Ser Gly Thr Tyr Glu Lys Cys Asn
85 90 95
Asp Ser Ser Val Tyr Tyr Asn Leu Thr Ser Gln Ser Gln Ser Val Phe
100 105 110
Gln Thr Asn Trp Thr Val Pro Thr Ser Glu Asp Val Thr Lys Val Asn
115 120 125
Leu Gln Val Leu Ile Val Val Asn Arg Thr Ala Ser Lys Ser Ser Val
130 135 140
Lys Met Glu Gln Val Gln Pro Ser Ala Ser Thr Pro Ile Pro Glu Ser
145 150 155 160
Ser Glu Thr Ser Gln Thr Ile Asn Thr Thr Pro Thr Val Asn Thr Ala
165 170 175
Lys Thr Thr Ala Lys Asp Thr Ala Asn Thr Thr Ala Val Thr Thr Ala
180 185 190
Asn Thr Thr Ala Asn Thr Thr Ala Val Thr Thr Ala Lys Thr Thr Ala
195 200 205
Lys Ser Leu Ala Ile Arg Thr
210 215

<210> 348
<211> 21
<212> PRT
<213> Mouse

<400> 348
Gly Tyr Ser Asp Gly Tyr Gln Val Cys Ser Arg Phe Gly Ser Lys Val
1 5 10 15
Pro Gln Phe Leu Asn

<210> 349

<211> 417
<212> DNA
<213> Mouse

<400> 349
gctagccgtg cacccagctc tccggagcgc gtgcaggcga gccgagcgcc ccgtccgcgg 60
ttctcgggca ggcgctgcgg gctccccggc tccccgccgt cccgggcacc cgggcgggcc 120
atgcgcccgg gctagagcgt agccgccggc atgccgctcc cgctgctgct cgccgcgctc 180
tgcctcgccg cctccccggc gcccgcgcgc gcctgccagc tgccgtcgga gtggagaccc 240
ttgagcgaag gctgccgcgc cgagctagcc gagaccatcg tgtatgccaa ggtgctggcg 300
ctgcaccccg aggtgcctgg cctctacaac tacctgccgt ggcagtacca agctggagag 360
ggagggctct tctactccgc cgaggtggag atgcttgtgt gaccaaggcg tggggca 417

<210> 350
<211> 1837
<212> DNA
<213> Mouse

<400> 350
cccccacctg cccagccaag ccgagtgccg ccggctttgt tcgctttgtc ctcgcgcacc 60
taagcggccg gcctggaaga acgccatccc ggagagcgca cgcggcgtcg caccaggtct 120
aacaacatgc ctccacttct gcttctacca gccatctaca tgctcctgtt cttcagagtg 180
tccccgacca tctctcttca ggaagtgcat gtgaaccggg agaccatggg gaagatcgct 240
gtggccagca aattaatgtg gtgctcagcc gcggtcgaca tcctgtttct gttagatggc 300
tctcacagca tcgggaaggg gagcttcgag aggtccaagc gcttcgccat cgctgcctgt 360
gatgccctgg acatcagccc tggcagggtc agagtcggag ccttgcagtt tggttccact 420
cctcatctgg aattcccctt ggactccttc tcaactcgac aggaagtgaa ggaaagcatc 480
aaggggatag ttttcaaagg tgggcgcacc gagacgggcc tagccctgaa acgcctgagc 540
agagggttcc ccggaggcag aaatggctct gtgccccaga ttcttatcat cgtcacggat 600
ggcaagtccc aggggcccgt ggctctcccg gctaagcagc tgagagaaag ggcatcgtc 660
gtgtttgccg taggagtccg ttttcccagg tgggacgagc tgctcacgct ggccagtgag 720
ccgaaggacc ggcatgtgct gttggctgag caagtggagg atgccaccaa tggcctcctc 780
agcaccctca gcagctccgc actctgcacc actgctgatc cagactgcag ggtggaacct 840
catccctgtg agcggaggac gctggagacc gtcagggagc tcgctggcaa tgccttgtgc 900
tggagaggat caaggcaagc agacactgtg ctggctctgc cctgtccctt ctacagctgg 960
aagagagtgt tccagacaca ccctgccaac tgctacagaa ccatctgtcc aggcccctgt 1020
gactcccagc cctgccaaaa tggaggcacg tgcattccag aaggtgtgga taggtaccac 1080
tgtctctgcc cactggcatt cggaggggaa gtcaactgtg ccccgaagct gagcctggaa 1140
tgcagaatcg atgtcctctt cctgctggac agttctgcag gcaccacatt gggggcttc 1200
cggagggcca aggcctttgt caagcgcttt gtgcaggccg tgctgaggga ggactcccga 1260
gcccgcgttg ggatagccag ttatggcagg aatctaatgg tggcggtgcc ctgtcgggga 1320
gtaccagcat tgtgccggac ctgatcagga gccttgacag cattcccttc agcggtggcc 1380
cgaccctaac cgggagtgcc ttgctccagg tggcagagca cggctttggg agtgccagca 1440
ggactggtca ggacaggcca cgcagagtag tagttctgct cactgaatca cgctcccagg 1500
atgaggtgtc tgggccagca gctcacgcaa gggctcggga gctactcctc ctgggcgtgg 1560
gcagtgagat cctgcaggcg gagctggtga agatcaccgg tagcccgaag catgtgatgg 1620
tccacacaga ccctcaggac ctgtcagcca aatccagagc tgcagaggag gctatgcagc 1680
cagccacggc caggctgcca ggcacagtca ctggacctgg tcttcctgtg gatgcctctg 1740
ctctgtggga cgtgagaact ttgcccaaat gcagagcttc atcaggaaat gcaccctccg 1800
gtttgatgtg aatcctgatg tgacacaagt tggcctg 1837

<210> 351
<211> 941
<212> DNA
<213> Mouse

<400> 351
taagccctca ggccctccta atgctatccc cctttgttcc tgcagcgtgg acccagtcag 60
cagccaggcc atggagctct ctgatgtcac cctcattgag ggtgtgggta acgaggtgat 120
ggtggtagca ggcgtggtgg cgctgactct agccctggtc ctagcctggc tctccaccta 180
tgtagcagac agtggtaaca accagctgct gggcaccatt gtgtcagcag gtgacacgtc 240

tgttctccac ctgggccatg tggaccagct ggtaaaccaa ggcactccag agccaaccga 300
acaccccccat ccatcagggg gcaatgatga caaggctgaa gagaccagtg acagtggggg 360
agacgccact ggagaacctg gagctagggg agagatggag cccagcctgg agcatctcct 420
ggacatccaa ggcctgccta aaaggcaagc aggcctgggg agcagtcgcc cagaagcccc 480
gctggggtta gatgatggct cctgcctctc tcccagcccc agcctcatca atgttcgcct 540
caagttcctc aatgacacgg aggagctagc tgtggccagg ccagaggaca ctgtgggtac 600
cctaaaaagg tgagtaggcc ggagagaggc cagttgctcg tgacttgttc ctcagatgat 660
ggtttcctga agaagctgtg catatatgtg agcacaggag ggattttaag ggaaatgga 720
gacttccata gacagacctt cagtgtcttt catgtccagg ccttgatctc tctagcctta 780
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<212> DNA
<213> Rat

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<211> 528
<212> DNA
<213> Rat

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<213> Mouse

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<210> 356
<211> 431
<212> DNA
<213> Rat

<400> 356
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<210> 357
<211> 1206
<212> DNA
<213> Mouse

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<211> 1052
<212> DNA

<213> Rat

<400> 358

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<400> 359

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<212> DNA
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<400> 360

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<211> 495
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<213> Mouse

<400> 361
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<210> 362
<211> 349
<212> DNA
<213> Mouse

<400> 362
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<211> 380
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<213> Mouse

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<211> 351
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<211> 854
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<213> Rat

<400> 365
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<210> 366
<211> 257
<212> DNA
<213> Rat

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<210> 367
<211> 475
<212> DNA
<213> Rat

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<212> DNA
<213> Mouse

<400> 368
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<210> 369
<211> 824
<212> DNA
<213> Rat

<400> 369

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<210> 370
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<212> DNA
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<400> 370

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aaagtgcact ccccctcagt gaatacgcaa acagcactgt tctctgagtt aggatgttag   1440
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<210> 371
<211> 568
<212> DNA
<213> Human

<400> 371
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gtgactgtaa cacctccaat cacagcccag caaggtaact ggacagttaa caaaacagaa 180
gctgacaaca tagaaggacc catagccttg aagttctcac acctttgcct ggaagatcat 240
aacagttact gcatcaacgg tgcttgtgca ttccaccatg agctagagaa agccatctgc 300
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ttttcagatg aaacaacaaa acttgtcaag ctgactagac tcgaaaataa tgaaagttgg 480
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ggagtgatgg aagccaagtg aacaagcc 568

<210> 372
<211> 5583
<212> DNA
<213> Rat

<400> 372
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<210> 373

<211> 83
<212> PRT
<213> Mouse

<400> 373
Met Pro Leu Pro Leu Leu Leu Ala Ala Leu Cys Leu Ala Ala Ser Pro
1 5 10 15
Ala Pro Ala Arg Ala Cys Gln Leu Pro Ser Glu Trp Arg Pro Leu Ser
20 25 30
Glu Gly Cys Arg Ala Glu Leu Ala Glu Thr Ile Val Tyr Ala Lys Val
35 40 45
Leu Ala Leu His Pro Glu Val Pro Gly Leu Tyr Asn Tyr Leu Pro Trp
50 55 60
Gln Tyr Gln Ala Gly Glu Gly Gly Leu Phe Tyr Ser Ala Glu Val Glu
65 70 75 80
Met Leu Val

<210> 374
<211> 405
<212> PRT
<213> Mouse

<400> 374
Met Pro Pro Leu Leu Leu Leu Pro Ala Ile Tyr Met Leu Leu Phe Phe
1 5 10 15
Arg Val Ser Pro Thr Ile Ser Leu Gln Glu Val His Val Asn Arg Glu
20 25 30
Thr Met Gly Lys Ile Ala Val Ala Ser Lys Leu Met Trp Cys Ser Ala
35 40 45
Ala Val Asp Ile Leu Phe Leu Leu Asp Gly Ser His Ser Ile Gly Lys
50 55 60
Gly Ser Phe Glu Arg Ser Lys Arg Phe Ala Ile Ala Ala Cys Asp Ala
65 70 75 80
Leu Asp Ile Ser Pro Gly Arg Val Arg Val Gly Ala Leu Gln Phe Gly
85 90 95
Ser Thr Pro His Leu Glu Phe Pro Leu Asp Ser Phe Ser Thr Arg Gln
100 105 110
Glu Val Lys Glu Ser Ile Lys Gly Ile Val Phe Lys Gly Gly Arg Thr
115 120 125
Glu Thr Gly Leu Ala Leu Lys Arg Leu Ser Arg Gly Phe Pro Gly Gly
130 135 140
Arg Asn Gly Ser Val Pro Gln Ile Leu Ile Ile Val Thr Asp Gly Lys
145 150 155 160
Ser Gln Gly Pro Val Ala Leu Pro Ala Lys Gln Leu Arg Glu Arg Gly
165 170 175
Ile Val Val Phe Ala Val Gly Val Arg Phe Pro Arg Trp Asp Glu Leu
180 185 190
Leu Thr Leu Ala Ser Glu Pro Lys Asp Arg His Val Leu Leu Ala Glu
195 200 205
Gln Val Glu Asp Ala Thr Asn Gly Leu Leu Ser Thr Leu Ser Ser Ser
210 215 220
Ala Leu Cys Thr Thr Ala Asp Pro Asp Cys Arg Val Glu Pro His Pro
225 230 235 240
Cys Glu Arg Arg Thr Leu Glu Thr Val Arg Glu Leu Ala Gly Asn Ala
245 250 255
Leu Cys Trp Arg Gly Ser Arg Gln Ala Asp Thr Val Leu Ala Leu Pro
260 265 270
Cys Pro Phe Tyr Ser Trp Lys Arg Val Phe Gln Thr His Pro Ala Asn
275 280 285
Cys Tyr Arg Thr Ile Cys Pro Gly Pro Cys Asp Ser Gln Pro Cys Gln

```
    290                 295                 300
Asn Gly Gly Thr Cys Ile Pro Glu Gly Val Asp Arg Tyr His Cys Leu
305                 310                 315                 320
Cys Pro Leu Ala Phe Gly Gly Glu Val Asn Cys Ala Pro Lys Leu Ser
                325                 330                 335
Leu Glu Cys Arg Ile Asp Val Leu Phe Leu Leu Asp Ser Ser Ala Gly
            340                 345                 350
Thr Thr Leu Gly Gly Phe Arg Arg Ala Lys Ala Phe Val Lys Arg Phe
        355                 360                 365
Val Gln Ala Val Leu Arg Glu Asp Ser Arg Ala Arg Val Gly Ile Ala
    370                 375                 380
Ser Tyr Gly Arg Asn Leu Met Val Ala Val Pro Cys Arg Gly Val Pro
385                 390                 395                 400
Ala Leu Cys Arg Thr
                405

      <210> 375
      <211> 180
      <212> PRT
      <213> Mouse

      <400> 375
Met Glu Leu Ser Asp Val Thr Leu Ile Glu Gly Val Gly Asn Glu Val
 1               5                  10                  15
Met Val Val Ala Gly Val Val Ala Leu Thr Leu Ala Leu Val Leu Ala
            20                  25                  30
Trp Leu Ser Thr Tyr Val Ala Asp Ser Gly Asn Asn Gln Leu Leu Gly
        35                  40                  45
Thr Ile Val Ser Ala Gly Asp Thr Ser Val Leu His Leu Gly His Val
    50                  55                  60
Asp Gln Leu Val Asn Gln Gly Thr Pro Glu Pro Thr Glu His Pro His
65                  70                  75                  80
Pro Ser Gly Gly Asn Asp Asp Lys Ala Glu Glu Thr Ser Asp Ser Gly
                85                  90                  95
Gly Asp Ala Thr Gly Glu Pro Gly Ala Arg Gly Glu Met Glu Pro Ser
            100                 105                 110
Leu Glu His Leu Leu Asp Ile Gln Gly Leu Pro Lys Arg Gln Ala Gly
        115                 120                 125
Leu Gly Ser Ser Arg Pro Glu Ala Pro Leu Gly Leu Asp Asp Gly Ser
    130                 135                 140
Cys Leu Ser Pro Ser Pro Ser Leu Ile Asn Val Arg Leu Lys Phe Leu
145                 150                 155                 160
Asn Asp Thr Glu Glu Leu Ala Val Ala Arg Pro Glu Asp Thr Val Gly
                165                 170                 175
Thr Leu Lys Arg
            180

      <210> 376
      <211> 68
      <212> PRT
      <213> Mouse

      <400> 376
Met Cys Leu Pro Val Thr Val Trp Cys His Trp Ala Leu Trp Val Ala
 1               5                  10                  15
His Leu Pro Leu Ile Pro Ser Val Gly Lys Ser Gln Cys Thr Gln Met
            20                  25                  30
Trp His Cys Cys Met Pro Trp Val Cys Val Gly Asp Cys Leu Cys Leu
        35                  40                  45
Ser Asp Pro Leu Trp Leu Cys Leu Leu Lys Glu Thr Glu Thr Pro Cys
    50                  55                  60
```

Gly Phe Leu Ser
65

<210> 377
<211> 107
<212> PRT
<213> Rat

<400> 377
Met Pro Phe Arg Leu Leu Ile Pro Leu Gly Leu Val Cys Val Leu Leu
1 5 10 15
Pro Leu His His Gly Ala Pro Gly Pro Glu Gly Thr Ala Pro Asp Pro
20 25 30
Ala His Tyr Arg Glu Arg Val Lys Ala Met Phe Tyr His Ala Tyr Asp
35 40 45
Ser Tyr Leu Glu Asn Ala Phe Pro Tyr Asp Glu Leu Arg Pro Leu Thr
50 55 60
Cys Asp Gly His Asp Thr Trp Gly Ser Phe Ser Leu Thr Leu Ile Asp
65 70 75 80
Ala Leu Asp Thr Leu Leu Ile Leu Gly Asn Thr Ser Glu Phe Gln Arg
85 90 95
Val Val Glu Val Leu Gln Asp Lys Arg Gly Leu
100 105

<210> 378
<211> 95
<212> PRT
<213> Rat

<400> 378
Met Trp Phe Leu Pro Cys Ser Val Pro Leu Val Ile Ser Ser Cys His
1 5 10 15
Ser Gln Ala Ser Pro His Trp Pro Tyr Gly Ile Ile Ser Gly Gly Gln
20 25 30
Glu Gly Leu Cys Arg Leu Trp Thr Ala Thr Cys His Ser Arg Gly Glu
35 40 45
Ser Glu Val Ser Arg Ser Ser Arg Lys Glu Asp Pro Arg Ile Pro Gln
50 55 60
Gly Ser Leu Ser Gly Asn Val Asp Phe Trp Arg Val Cys Pro Pro Cys
65 70 75 80
Ala His Thr Ser Met Asp Arg Thr Leu Gly Leu Leu Ser Cys Cys
85 90 95

<210> 379
<211> 138
<212> PRT
<213> Mouse

<400> 379
Met Asp Leu Asp Val Val Asn Met Phe Val Ile Ala Gly Gly Thr Leu
1 5 10 15
Ala Ile Pro Ile Leu Ala Phe Val Ala Ser Phe Leu Leu Trp Pro Ser
20 25 30
Ala Leu Ile Arg Ile Tyr Tyr Trp Tyr Trp Arg Arg Thr Leu Gly Met
35 40 45
Gln Val Arg Tyr Ala His His Glu Asp Tyr Gln Phe Cys Tyr Ser Phe
50 55 60
Arg Gly Arg Pro Gly His Lys Pro Ser Ile Leu Met Leu His Gly Phe
65 70 75 80
Ser Ala His Lys Asp Met Trp Leu Ser Val Val Lys Phe Leu Pro Lys
85 90 95

```
Asn Leu His Leu Val Cys Val Asp Met Pro Gly His Glu Gly Thr Thr
            100                 105                 110
Arg Ser Ser Leu Asp Asp Leu Ser Ile Val Gly Gln Val Lys Arg Ile
        115                 120                 125
His Gln Phe Val Glu Cys Leu Lys Leu Asn
    130                 135

      <210> 380
      <211> 81
      <212> PRT
      <213> Rat

      <400> 380
Met Ala Ser Ser Ser Asn Trp Leu Ser Gly Val Asn Val Val Leu Val
 1               5                  10                  15
Met Ala Tyr Gly Ser Leu Val Phe Val Leu Leu Phe Ile Phe Val Lys
            20                  25                  30
Arg Gln Ile Met Arg Phe Ala Met Lys Ser Arg Arg Gly Pro His Val
        35                  40                  45
Pro Val Gly His Asn Ala Pro Lys Asp Leu Lys Glu Glu Ile Asp Ile
    50                  55                  60
Arg Leu Ser Arg Val Gln Asp Ile Lys Tyr Glu Pro Gln Leu Leu Ala
65                  70                  75                  80
Asp


      <210> 381
      <211> 257
      <212> PRT
      <213> Mouse

      <400> 381
Met Arg Ser Gly Ala Leu Trp Pro Leu Leu Trp Gly Ala Leu Val Trp
 1               5                  10                  15
Thr Val Gly Ser Val Gly Ala Val Met Gly Ser Glu Asp Ser Val Pro
            20                  25                  30
Gly Gly Val Cys Trp Leu Gln Gln Gly Arg Glu Ala Thr Cys Ser Leu
        35                  40                  45
Val Leu Lys Thr Arg Val Ser Arg Glu Glu Cys Cys Ala Ser Gly Asn
    50                  55                  60
Ile Asn Thr Ala Trp Ser Asn Phe Thr His Pro Gly Asn Lys Ile Ser
65                  70                  75                  80
Leu Leu Gly Phe Leu Gly Leu Val His Cys Leu Pro Cys Lys Asp Ser
                85                  90                  95
Cys Asp Gly Val Glu Cys Gly Pro Gly Lys Ala Cys Arg Met Leu Gly
            100                 105                 110
Gly Arg Pro Thr Leu Arg Ser Cys Val Pro Asn Cys Glu Gly Leu Pro
        115                 120                 125
Ala Gly Phe Gln Val Cys Gly Ser Asp Gly Ala Thr Tyr Arg Asp Glu
    130                 135                 140
Cys Glu Leu Arg Thr Ala Arg Cys Arg Gly His Pro Asp Leu Arg Val
145                 150                 155                 160
Met Tyr Arg Gly Arg Cys Gln Lys Ser Cys Ala Gln Val Val Cys Pro
                165                 170                 175
Arg Pro Gln Ser Cys Leu Val Asp Gln Thr Gly Ser Ala His Cys Val
            180                 185                 190
Val Cys Arg Ala Ala Pro Cys Pro Val Pro Ser Asn Pro Gly Gln Glu
        195                 200                 205
Leu Cys Gly Asn Asn Asn Val Thr Tyr Ile Ser Ser Cys His Leu Arg
    210                 215                 220
Gln Ala Thr Cys Phe Leu Gly Arg Ser Ile Gly Val Arg His Pro Gly
```

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225                 230                 235                 240
Ile Cys Thr Gly Gly Pro Lys Val Pro Ala Glu Glu Glu Glu Asn Phe
                245                 250                 255
Val


      <210> 382
      <211> 285
      <212> PRT
      <213> Rat

      <400> 382
Met Ile Ser Trp Met Leu Leu Ala Cys Ala Leu Pro Cys Ala Ala Asp
 1               5                  10                  15
Pro Met Leu Gly Ala Phe Ala Arg Arg Asp Phe Gln Lys Gly Gly Pro
            20                  25                  30
Gln Leu Val Cys Ser Leu Pro Gly Pro Gln Gly Pro Pro Gly Pro Pro
        35                  40                  45
Gly Ala Pro Gly Ser Ser Gly Met Val Gly Arg Met Gly Phe Pro Gly
    50                  55                  60
Lys Asp Gly Gln Asp Gly Gln Asp Gly Asp Arg Gly Asp Ser Gly Glu
65                  70                  75                  80
Glu Gly Pro Pro Gly Arg Thr Gly Asn Arg Gly Lys Gln Gly Pro Lys
                85                  90                  95
Gly Lys Ala Gly Ala Ile Gly Arg Ala Gly Pro Arg Gly Pro Lys Gly
            100                 105                 110
Val Ser Gly Thr Pro Gly Lys His Gly Ile Pro Gly Lys Lys Gly Pro
        115                 120                 125
Lys Gly Lys Lys Gly Glu Pro Gly Leu Pro Gly Pro Cys Ser Cys Gly
    130                 135                 140
Ser Ser Arg Ala Lys Ser Ala Phe Ser Val Ser Val Thr Lys Ser Tyr
145                 150                 155                 160
Pro Arg Glu Arg Leu Pro Ile Lys Phe Asp Lys Ile Leu Met Asn Glu
                165                 170                 175
Gly Gly His Tyr Asn Ala Ser Ser Gly Lys Phe Val Cys Ser Val Pro
            180                 185                 190
Gly Ile Tyr Tyr Phe Thr Tyr Asp Ile Thr Leu Ala Asn Lys His Leu
        195                 200                 205
Ala Ile Gly Leu Val His Asn Gly Gln Tyr Arg Ile Arg Thr Phe Asp
    210                 215                 220
Ala Asn Thr Gly Asn His Asp Val Ala Ser Gly Ser Thr Ile Leu Ala
225                 230                 235                 240
Leu Lys Glu Gly Asp Glu Val Trp Leu Gln Ile Phe Tyr Ser Glu Gln
                245                 250                 255
Asn Gly Leu Phe Tyr Asp Pro Tyr Trp Thr Asp Ser Leu Phe Thr Gly
            260                 265                 270
Phe Leu Ile Tyr Ala Asp Gln Gly Asp Pro Asn Glu Val
        275                 280                 285

      <210> 383
      <211> 183
      <212> PRT
      <213> Rat

      <400> 383
Met Lys Leu Leu Cys Leu Val Ala Val Val Gly Cys Leu Leu Val Pro
 1               5                  10                  15
Pro Ala Gln Ala Asn Lys Ser Ser Glu Asp Ile Arg Cys Lys Cys Ile
            20                  25                  30
Cys Pro Pro Tyr Arg Asn Ile Ser Gly His Ile Tyr Asn Gln Asn Val
        35                  40                  45
```

```
Ser Gln Lys Asp Cys Asn Cys Leu His Val Val Glu Pro Met Pro Val
    50                  55                  60
Pro Gly His Asp Val Glu Ala Tyr Cys Leu Leu Cys Glu Cys Arg Tyr
65                  70                  75                  80
Glu Glu Arg Ser Thr Thr Thr Ile Lys Val Ile Ile Val Ile Tyr Leu
                85                  90                  95
Ser Val Val Gly Ala Leu Leu Leu Tyr Met Ala Phe Leu Met Leu Val
            100                 105                 110
Asp Pro Leu Ile Arg Lys Pro Asp Ala Tyr Thr Glu Gln Leu His Asn
        115                 120                 125
Glu Glu Glu Asn Glu Asp Ala Arg Ser Met Ala Ala Ala Ala Ala Ser
    130                 135                 140
Ile Gly Gly Pro Arg Ala Asn Thr Val Leu Glu Arg Val Glu Gly Ala
145                 150                 155                 160
Gln Gln Arg Trp Lys Leu Gln Val Gln Glu Gln Arg Lys Thr Val Phe
                165                 170                 175
Asp Arg His Lys Met Leu Ser
            180
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<210> 384
<211> 292
<212> PRT
<213> Mouse

<400> 384

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Cys Gln Leu Pro Leu Arg Val Leu Ile Ile Ser Asn Asn Lys Leu Gly
 1               5                  10                  15
Ala Leu Pro Pro Asp Ile Ser Thr Leu Gly Ser Leu Arg Gln Leu Asp
            20                  25                  30
Val Ser Ser Asn Glu Leu Gln Ser Leu Pro Val Glu Leu Cys Ser Leu
        35                  40                  45
Arg Ser Leu Arg Asp Leu Asn Val Arg Arg Asn Gln Leu Ser Thr Leu
    50                  55                  60
Pro Asp Glu Leu Gly Asp Leu Pro Leu Val Arg Leu Asp Phe Ser Cys
65                  70                  75                  80
Asn Arg Ile Ser Arg Ile Pro Val Ser Phe Cys Arg Leu Arg His Leu
                85                  90                  95
Gln Val Val Leu Leu Asp Ser Asn Pro Leu Gln Ser Pro Pro Ala Gln
            100                 105                 110
Ile Cys Leu Lys Gly Lys Leu His Ile Phe Lys Tyr Leu Thr Met Glu
        115                 120                 125
Ala Gly Arg Arg Gly Ala Ala Leu Gly Asp Leu Val Pro Ser Arg Pro
    130                 135                 140
Pro Ser Phe Ser Pro Cys Pro Ala Glu Asp Leu Phe Pro Gly Arg Arg
145                 150                 155                 160
Tyr Asp Gly Gly Leu Asp Ser Gly Phe His Ser Val Asp Ser Gly Ser
                165                 170                 175
Lys Arg Trp Ser Gly Asn Glu Ser Thr Asp Asp Phe Ser Glu Leu Ser
            180                 185                 190
Phe Arg Ile Ser Glu Leu Ala Arg Asp Pro Arg Gly Pro Arg Gln Pro
        195                 200                 205
Arg Glu Asp Gly Ala Gly Asp Gly Asp Leu Glu Gln Ile Asp Phe Ile
    210                 215                 220
Asp Ser His Val Pro Gly Glu Asp Glu Asp Arg Ser Ala Ala Glu Glu
225                 230                 235                 240
Gln Leu Pro Ser Glu Leu Ser Leu Val Ala Gly Asp Val Glu Lys Pro
                245                 250                 255
Ser Ser Ser Arg Arg Glu Glu Pro Ala Gly Glu Glu Arg Arg Arg Pro
            260                 265                 270
Asp Thr Leu Gln Leu Trp Gln Glu Arg Glu Arg Lys Gln Gln Gln Gln
        275                 280                 285
```

```
Ser Gly Gly Trp
    290

      &lt;210&gt; 385
      &lt;211&gt; 164
      &lt;212&gt; PRT
      &lt;213&gt; Mouse

      &lt;400&gt; 385
Ser Arg Gln Leu Arg Ala Pro Arg Phe Asp Pro Arg Ala Gly Phe His
 1               5                  10                  15
Ala Glu Gly Lys Asp Arg Gly Pro Ser Val Pro Gln Gly Leu Leu Lys
            20                  25                  30
Ala Ala Arg Ser Ser Gly Gln Leu Asn Leu Ala Gly Arg Asn Leu Gly
        35                  40                  45
Glu Val Pro Gln Cys Val Trp Arg Ile Asn Val Asp Ile Pro Glu Glu
    50                  55                  60
Ala Asn Gln Asn Leu Ser Phe Ser Ser Thr Glu Arg Trp Trp Asp Gln
65                  70                  75                  80
Thr Asp Leu Thr Lys Leu Ile Ile Ser Ser Asn Lys Leu Gln Ser Leu
                85                  90                  95
Ser Asp Asp Leu Arg Leu Leu Pro Ala Leu Thr Val Leu Asp Ile His
            100                 105                 110
Asp Asn Gln Leu Thr Ser Leu Pro Ser Ala Ile Arg Glu Leu Asp Asn
        115                 120                 125
Leu Gln Lys Leu Asn Val Ser His Asn Lys Leu Lys Ile Leu Pro Glu
    130                 135                 140
Glu Ile Thr Ser Leu Lys Asn Leu Arg Thr Leu His Leu Gln His Asn
145                 150                 155                 160
Glu Leu Thr Cys


      &lt;210&gt; 386
      &lt;211&gt; 71
      &lt;212&gt; PRT
      &lt;213&gt; Mouse

      &lt;400&gt; 386
Ser Leu Ser Ile Leu Pro Ala Val Arg Val Ser Pro Arg Pro Thr Tyr
 1               5                  10                  15
Pro Ser Thr Ala Ser Ser Met Ala Ala Phe Leu Val Thr Gly Phe Phe
            20                  25                  30
Phe Ser Leu Phe Val Val Leu Gly Met Glu Pro Arg Ala Leu Phe Arg
        35                  40                  45
Pro Asp Lys Ala Leu Pro Leu Ser Cys Ala Lys Pro Thr Ser Leu Cys
    50                  55                  60
Val Gln Ser Ser Phe Leu Gly
65                  70

      &lt;210&gt; 387
      &lt;211&gt; 126
      &lt;212&gt; PRT
      &lt;213&gt; Mouse

      &lt;400&gt; 387
Glu Tyr Glu Ala Arg Val Leu Glu Lys Ser Leu Arg Lys Glu Ser Arg
 1               5                  10                  15
Asn Lys Glu Thr Asp Lys Val Lys Leu Thr Trp Arg Asp Arg Phe Pro
            20                  25                  30
Ala Tyr Phe Thr Asn Leu Val Ser Ile Ile Phe Met Ile Ala Val Thr
        35                  40                  45
```

Phe Ala Ile Val Leu Gly Val Ile Ile Tyr Arg Ile Ser Thr Ala Ala
50 55 60
Ala Leu Ala Met Asn Ser Ser Pro Ser Val Arg Ser Asn Ile Arg Val
65 70 75 80
Thr Val Thr Ala Thr Ala Val Ile Ile Asn Leu Val Val Ile Ile Leu
85 90 95
Leu Asp Glu Val Tyr Gly Cys Ile Ala Arg Trp Leu Thr Lys Ile Gly
100 105 110
Glu Cys His Val Gln Asp Ser Ile Gly Ser Met Gly Leu Gly
115 120 125

<210> 388
<211> 84
<212> PRT
<213> Rat

<400> 388
Ala Ala Glu Asn Glu Met Pro Val Ala Val Gly Pro Tyr Gly Gln Ser
1 5 10 15
Gln Pro Ser Cys Phe Asp Arg Val Lys Met Gly Phe Val Met Gly Cys
20 25 30
Ala Val Gly Met Ala Ala Gly Ala Leu Phe Gly Thr Phe Ser Cys Leu
35 40 45
Arg Ile Gly Met Arg Gly Arg Glu Leu Met Gly Gly Ile Gly Lys Thr
50 55 60
Met Met Gln Ser Gly Gly Thr Phe Gly Thr Phe Met Ala Ile Gly Met
65 70 75 80
Gly Ile Arg Cys

<210> 389
<211> 284
<212> PRT
<213> Rat

<400> 389
Gly Gly Ser Ser Val Ser His Val Leu Arg Gly Ser Gly Gln Glu Arg
1 5 10 15
Ser Pro Pro Pro Ala Ser Met Gln Pro Pro Trp Gly Leu Ala Leu Pro
20 25 30
Leu Leu Leu Pro Trp Val Ala Gly Gly Val Gly Thr Ser Pro Arg Asp
35 40 45
Tyr Trp Leu Pro Ala Leu Ala His Gln Pro Gly Val Cys His Tyr Gly
50 55 60
Thr Lys Thr Ala Cys Cys Tyr Gly Trp Lys Arg Asn Ser Lys Gly Val
65 70 75 80
Cys Glu Ala Val Cys Glu Pro Arg Cys Lys Phe Gly Glu Cys Val Gly
85 90 95
Pro Asn Lys Cys Arg Cys Phe Pro Gly Tyr Thr Gly Lys Thr Cys Ser
100 105 110
Gln Asp Val Asn Glu Cys Ala Phe Lys Pro Arg Pro Cys Gln His Arg
115 120 125
Cys Val Asn Thr His Gly Ser Tyr Lys Cys Phe Cys Leu Ser Gly His
130 135 140
Met Leu Leu Pro Asp Ala Thr Cys Ser Asn Ser Arg Thr Cys Ala Arg
145 150 155 160
Ile Asn Cys Gln Tyr Ser Cys Glu Asp Thr Ala Glu Gly Pro Arg Cys
165 170 175
Val Cys Pro Ser Ser Gly Leu Arg Leu Gly Pro Asn Gly Arg Val Cys
180 185 190
Leu Asp Ile Asp Glu Cys Ala Ser Ser Lys Ala Val Cys Pro Ser Asn

195 200 205
Arg Arg Cys Val Asn Thr Phe Gly Ser Tyr Tyr Cys Lys Cys His Ile
210 215 220
Gly Phe Glu Leu Lys Tyr Ile Ser Arg Arg Tyr Asp Cys Val Asp Ile
225 230 235 240
Asn Glu Cys Thr Leu Asn Thr Arg Thr Cys Ser Pro His Ala Asn Cys
245 250 255
Leu Asn Thr Gln Gly Ser Phe Lys Cys Lys Cys Lys Gln Gly Tyr Arg
260 265 270
Gly Asn Gly Leu Gln Cys Ser Val Ile Pro Glu His
275 280

<210> 390
<211> 85
<212> PRT
<213> Rat

<400> 390
Gly Ala Pro Met Tyr Phe Ser Glu Gly Arg Glu Arg Gly Lys Val Tyr
1 5 10 15
Val Tyr Asn Leu Arg Gln Asn Arg Phe Val Phe Asn Gly Thr Leu Lys
20 25 30
Asp Ser His Ser Tyr Gln Asn Ala Arg Phe Gly Ser Cys Ile Ala Ser
35 40 45
Val Gln Asp Leu Asn Gln Asp Ser Tyr Asn Asp Val Val Val Gly Ala
50 55 60
Pro Gln Glu Asp Ser His Arg Gly Ala Ile Tyr Ile Phe His Gly Phe
65 70 75 80
Gln Thr Asn Ile Leu
85

<210> 391
<211> 158
<212> PRT
<213> Rat

<400> 391
Phe Gln Thr Asn Ile Leu Lys Lys Pro Val Gln Arg Ile Ser Ala Ser
1 5 10 15
Glu Leu Ala Pro Gly Leu Gln His Phe Gly Cys Ser Ile His Gly Gln
20 25 30
Leu Asp Leu Asn Glu Asp Gly Leu Val Asp Leu Ala Val Gly Ala Leu
35 40 45
Gly Asn Ala Val Val Leu Trp Ala Arg Pro Val Val Gln Ile Asn Ala
50 55 60
Ser Leu His Phe Glu Pro Ser Lys Ile Asn Ile Phe His Lys Asp Cys
65 70 75 80
Lys Arg Asn Gly Arg Asp Ala Thr Cys Leu Ala Ala Phe Leu Cys Phe
85 90 95
Gly Pro Ile Phe Leu Ala Pro His Phe His Thr Ala Thr Val Gly Ile
100 105 110
Arg Tyr Asn Ala Thr Met Asp Glu Arg Arg Tyr Met Pro Arg Ala His
115 120 125
Leu Asp Glu Gly Ala Asp Gln Phe Thr Asn Arg Ala Val Leu Leu Ser
130 135 140
Ser Gly Gln Glu His Cys Gln Arg Ile Asn Phe His Val Leu
145 150 155

<210> 392
<211> 124
<212> PRT

<213> Mouse

<400> 392
Ala Ala Glu Gln Glu Ala Ser Ser Arg Arg Arg Arg Gly Gly Ala Gly
1 5 10 15
Pro Ala Leu Phe Ser Ser Gly Ser Leu Arg Ser Glu Pro Gln Pro Arg
20 25 30
Leu Pro Gln Ala Arg Ser Arg Pro Arg Pro Ser Phe Leu Gln Ala Arg
35 40 45
Ser Arg Pro Cys Leu Ser Gln Ala Cys Ser Pro Ala Ala Ser Val Leu
50 55 60
Ser Ser Ser Ser Leu Cys Gly Arg Ser His Leu Leu Pro Gly Ser Leu
65 70 75 80
Pro Ala Thr Ala Phe Leu Leu Leu Leu Pro Gly Ser Leu Pro Gly Arg
85 90 95
Arg Pro Ser Ala Ala Gln Ala Ala Pro Val Leu Ala Trp Gly Leu Val
100 105 110
Ala Phe Gln Leu Gly Val Ala Ala Gly Ala Gly Arg
115 120

<210> 393
<211> 242
<212> PRT
<213> Rat

<400> 393
Gly His Cys Asp Cys Gln Ala Gly Tyr Gly Gly Glu Ala Cys Gly Gln
1 5 10 15
Cys Gly Leu Gly Tyr Phe Glu Ala Glu Arg Asn Ser Ser His Leu Val
20 25 30
Cys Ser Ala Cys Phe Gly Pro Cys Ala Arg Cys Thr Gly Pro Glu Glu
35 40 45
Ser His Cys Leu Gln Cys Arg Lys Gly Trp Ala Leu His His Leu Lys
50 55 60
Cys Val Asp Ile Asp Glu Cys Gly Thr Glu Gln Ala Thr Cys Gly Ala
65 70 75 80
Asp Gln Phe Cys Val Asn Thr Glu Gly Ser Tyr Glu Cys Arg Asp Cys
85 90 95
Ala Lys Ala Cys Leu Gly Cys Met Gly Ala Gly Pro Gly Pro Cys Lys
100 105 110
Lys Cys Ser Arg Gly Tyr Gln Gln Val Gly Ser Lys Cys Leu Asp Val
115 120 125
Asp Glu Cys Glu Thr Val Val Cys Pro Gly Glu Asn Glu Gln Cys Glu
130 135 140
Asn Thr Glu Gly Ser Tyr Arg Cys Val Cys Ala Glu Gly Phe Arg Gln
145 150 155 160
Glu Asp Gly Ile Cys Val Lys Glu Gln Ile Pro Glu Ser Ala Gly Phe
165 170 175
Phe Ala Glu Met Thr Glu Asp Glu Met Val Val Leu Gln Gln Met Phe
180 185 190
Phe Gly Val Ile Ile Cys Ala Leu Ala Thr Leu Ala Ala Lys Gly Asp
195 200 205
Leu Val Phe Thr Ala Ile Phe Ile Gly Ala Val Ala Ala Met Thr Gly
210 215 220
Tyr Trp Leu Ser Glu Arg Ser Asp Arg Val Leu Glu Gly Phe Ile Lys
225 230 235 240
Gly Arg

<210> 394
<211> 99

<212> PRT
<213> Mouse

<400> 394
Met Arg Leu Leu Ala Ala Ala Leu Leu Leu Leu Leu Leu Ala Leu Cys
1 5 10 15
Ala Ser Arg Val Asp Gly Ser Lys Cys Lys Cys Ser Arg Lys Gly Pro
20 25 30
Lys Ile Arg Tyr Ser Asp Val Lys Lys Leu Glu Met Lys Pro Lys Tyr
35 40 45
Pro His Cys Glu Glu Lys Met Val Ile Val Thr Thr Lys Ser Met Ser
50 55 60
Arg Tyr Arg Gly Gln Glu His Cys Leu His Pro Lys Leu Gln Ser Thr
65 70 75 80
Lys Arg Phe Ile Lys Trp Tyr Asn Ala Trp Asn Glu Lys Arg Arg Val
85 90 95
Tyr Glu Glu

<210> 395
<211> 103
<212> PRT
<213> Human

<400> 395
Met Ala Leu Gly Val Pro Ile Ser Val Tyr Leu Leu Phe Asn Ala Met
1 5 10 15
Thr Ala Leu Thr Glu Glu Ala Ala Val Thr Val Thr Pro Pro Ile Thr
20 25 30
Ala Gln Gln Gly Asn Trp Thr Val Asn Lys Thr Glu Ala Asp Asn Ile
35 40 45
Glu Gly Pro Ile Ala Leu Lys Phe Ser His Leu Cys Leu Glu Asp His
50 55 60
Asn Ser Tyr Cys Ile Asn Gly Ala Cys Ala Phe His His Glu Leu Glu
65 70 75 80
Lys Ala Ile Cys Arg Cys Leu Lys Leu Lys Ser Pro Tyr Asn Val Cys
85 90 95
Ser Gly Glu Arg Arg Pro Leu
100

<210> 396
<211> 1529
<212> PRT
<213> Rat

<400> 396
Met Ser Gly Ile Gly Trp Gln Thr Leu Ser Leu Ser Leu Ala Leu Val
1 5 10 15
Leu Ser Ile Leu Asn Lys Val Ala Pro His Ala Cys Pro Ala Gln Cys
20 25 30
Ser Cys Ser Gly Ser Thr Val Asp Cys His Gly Leu Ala Leu Arg Ser
35 40 45
Val Pro Arg Asn Ile Pro Arg Asn Thr Glu Arg Leu Asp Leu Asn Gly
50 55 60
Asn Asn Ile Thr Arg Ile Thr Lys Thr Asp Phe Ala Gly Leu Arg His
65 70 75 80
Leu Arg Val Leu Gln Leu Met Glu Asn Lys Ile Ser Thr Ile Glu Arg
85 90 95
Gly Ala Phe Gln Asp Leu Lys Glu Leu Glu Arg Leu Arg Leu Asn Arg
100 105 110
Asn Asn Leu Gln Leu Phe Pro Glu Leu Leu Phe Leu Gly Thr Ala Lys

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        115                 120                 125
Leu Tyr Arg Leu Asp Leu Ser Glu Asn Gln Ile Gln Ala Ile Pro Arg
    130                 135                 140
Lys Ala Phe Arg Gly Ala Val Asp Ile Lys Asn Leu Gln Leu Asp Tyr
145                 150                 155                 160
Asn Gln Ile Ser Cys Ile Glu Asp Gly Ala Phe Arg Ala Leu Arg Asp
                165                 170                 175
Leu Glu Val Leu Thr Leu Asn Asn Asn Asn Ile Thr Arg Leu Ser Val
            180                 185                 190
Ala Ser Phe Asn His Met Pro Lys Leu Arg Thr Phe Arg Leu His Ser
        195                 200                 205
Asn Asn Leu Tyr Cys Asp Cys His Leu Ala Trp Leu Ser Asp Trp Leu
    210                 215                 220
Arg Gln Arg Pro Arg Val Gly Leu Tyr Thr Gln Cys Met Gly Pro Ser
225                 230                 235                 240
His Leu Arg Gly His Asn Val Ala Glu Val Gln Lys Arg Glu Phe Val
                245                 250                 255
Cys Ser Gly His Gln Ser Phe Met Ala Pro Ser Cys Ser Val Leu His
            260                 265                 270
Cys Pro Ile Ala Cys Thr Cys Ser Asn Asn Ile Val Asp Cys Arg Gly
        275                 280                 285
Lys Gly Leu Thr Glu Ile Pro Thr Asn Leu Pro Glu Thr Ile Thr Glu
    290                 295                 300
Ile Arg Leu Glu Gln Asn Ser Ile Arg Val Ile Pro Pro Gly Ala Phe
305                 310                 315                 320
Ser Pro Tyr Lys Lys Leu Arg Arg Leu Asp Leu Ser Asn Asn Gln Ile
                325                 330                 335
Ser Glu Leu Ala Pro Asp Ala Phe Gln Gly Leu Arg Ser Leu Asn Ser
            340                 345                 350
Leu Val Leu Tyr Gly Asn Lys Ile Thr Glu Leu Pro Lys Ser Leu Phe
        355                 360                 365
Glu Gly Leu Phe Ser Leu Gln Leu Leu Leu Leu Asn Ala Asn Lys Ile
    370                 375                 380
Asn Cys Leu Arg Val Asp Ala Phe Gln Asp Leu His Asn Leu Asn Leu
385                 390                 395                 400
Leu Ser Leu Tyr Asp Asn Lys Leu Gln Thr Val Ala Lys Gly Thr Phe
                405                 410                 415
Ser Ala Leu Arg Ala Ile Gln Thr Met His Leu Ala Gln Asn Pro Phe
            420                 425                 430
Ile Cys Asp Cys His Leu Lys Trp Leu Ala Asp Tyr Leu His Thr Asn
        435                 440                 445
Pro Ile Glu Thr Ser Gly Ala Arg Cys Thr Ser Pro Arg Arg Leu Ala
    450                 455                 460
Asn Lys Arg Ile Gly Gln Ile Lys Ser Lys Lys Phe Arg Cys Ser Ala
465                 470                 475                 480
Lys Glu Gln Tyr Phe Ile Pro Gly Thr Glu Asp Tyr Arg Ser Lys Leu
                485                 490                 495
Ser Gly Asp Cys Phe Ala Asp Leu Ala Cys Pro Glu Lys Cys Arg Cys
            500                 505                 510
Glu Gly Thr Thr Val Asp Cys Ser Asn Gln Lys Leu Asn Lys Ile Pro
        515                 520                 525
Asp His Ile Pro Gln Tyr Thr Ala Glu Leu Arg Leu Asn Asn Asn Glu
    530                 535                 540
Phe Thr Val Leu Glu Ala Thr Gly Ile Phe Lys Lys Leu Pro Gln Leu
545                 550                 555                 560
Arg Lys Ile Asn Leu Ser Asn Asn Lys Ile Thr Asp Ile Glu Glu Gly
                565                 570                 575
Ala Phe Glu Gly Ala Ser Gly Val Asn Glu Ile Leu Leu Thr Ser Asn
            580                 585                 590
Arg Leu Glu Asn Val Gln His Lys Met Phe Lys Gly Leu Glu Ser Leu
        595                 600                 605
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Lys Thr Leu Met Leu Arg Ser Asn Arg Ile Ser Cys Val Gly Asn Asp
    610                 615                 620
Ser Phe Thr Gly Leu Gly Ser Val Arg Leu Leu Ser Leu Tyr Asp Asn
625                 630                 635                 640
Gln Ile Thr Thr Val Ala Pro Gly Ala Phe Gly Thr Leu His Ser Leu
                645                 650                 655
Ser Thr Leu Asn Leu Leu Ala Asn Pro Phe Asn Cys Asn Cys His Leu
            660                 665                 670
Ala Trp Leu Gly Glu Trp Leu Arg Arg Lys Arg Ile Val Thr Gly Asn
        675                 680                 685
Pro Arg Cys Gln Lys Pro Tyr Phe Leu Lys Glu Ile Pro Ile Gln Asp
    690                 695                 700
Val Ala Ile Gln Asp Phe Thr Cys Asp Asp Gly Asn Asp Asp Asn Ser
705                 710                 715                 720
Cys Ser Pro Leu Ser Arg Cys Pro Ser Glu Cys Thr Cys Leu Asp Thr
                725                 730                 735
Val Val Arg Cys Ser Asn Lys Gly Leu Lys Val Leu Pro Lys Gly Ile
            740                 745                 750
Pro Arg Asp Val Thr Glu Leu Tyr Leu Asp Gly Asn Gln Phe Thr Leu
        755                 760                 765
Val Pro Lys Glu Leu Ser Asn Tyr Lys His Leu Thr Leu Ile Asp Leu
    770                 775                 780
Ser Asn Asn Arg Ile Ser Thr Leu Ser Asn Gln Ser Phe Ser Asn Met
785                 790                 795                 800
Thr Gln Leu Leu Thr Leu Ile Leu Ser Tyr Asn Arg Leu Arg Cys Ile
                805                 810                 815
Pro Pro Arg Thr Phe Asp Gly Leu Lys Ser Leu Arg Leu Leu Ser Leu
            820                 825                 830
His Gly Asn Asp Ile Ser Val Val Pro Glu Gly Ala Phe Gly Asp Leu
        835                 840                 845
Ser Ala Leu Ser His Leu Ala Ile Gly Ala Asn Pro Leu Tyr Cys Asp
    850                 855                 860
Cys Asn Met Gln Trp Leu Ser Asp Trp Val Lys Ser Glu Tyr Lys Glu
865                 870                 875                 880
Pro Gly Ile Ala Arg Cys Ala Gly Pro Gly Glu Met Ala Asp Lys Leu
                885                 890                 895
Leu Leu Thr Thr Pro Ser Lys Lys Phe Thr Cys Gln Gly Pro Val Asp
            900                 905                 910
Val Thr Ile Gln Ala Lys Cys Asn Pro Cys Leu Ser Asn Pro Cys Lys
        915                 920                 925
Asn Asp Gly Thr Cys Asn Asn Asp Pro Val Asp Phe Tyr Arg Cys Thr
    930                 935                 940
Cys Pro Tyr Gly Phe Lys Gly Gln Asp Cys Asp Val Pro Ile His Ala
945                 950                 955                 960
Cys Ile Ser Asn Pro Cys Lys His Gly Gly Thr Cys His Leu Lys Glu
                965                 970                 975
Gly Glu Asn Asp Gly Phe Trp Cys Thr Cys Ala Asp Gly Phe Glu Gly
            980                 985                 990
Glu Ser Cys Asp Ile Asn Ile Asp Asp Cys Glu Asp Asn Asp Cys Glu
        995                 1000                1005
Asn Asn Ser Thr Cys Val Asp Gly Ile Asn Asn Tyr Thr Cys Leu Cys
    1010                1015                1020
Pro Pro Glu Tyr Thr Gly Glu Leu Cys Glu Glu Lys Leu Asp Phe Cys
1025                1030                1035                104
Ala Gln Asp Leu Asn Pro Cys Gln His Asp Ser Lys Cys Ile Leu Thr
                1045                1050                1055
Pro Lys Gly Phe Lys Cys Asp Cys Thr Pro Gly Tyr Ile Gly Glu His
            1060                1065                1070
Cys Asp Ile Asp Phe Asp Asp Cys Gln Asp Asn Lys Cys Lys Asn Gly
        1075                1080                1085
Ala His Cys Thr Asp Ala Val Asn Gly Tyr Thr Cys Val Cys Pro Glu
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    1090                1095                1100
Gly Tyr Ser Gly Leu Phe Cys Glu Phe Ser Pro Pro Met Val Leu Leu
1105                1110                1115                112
Arg Thr Ser Pro Cys Asp Asn Phe Asp Cys Gln Asn Gly Ala Gln Cys
                1125                1130                1135
Ile Ile Arg Val Asn Glu Pro Ile Cys Gln Cys Leu Pro Gly Tyr Leu
            1140                1145                1150
Gly Glu Lys Cys Glu Lys Leu Val Ser Val Asn Phe Val Asn Lys Glu
        1155                1160                1165
Ser Tyr Leu Gln Ile Pro Ser Ala Lys Val Arg Pro Gln Thr Asn Ile
    1170                1175                1180
Thr Leu Gln Ile Ala Thr Asp Glu Asp Ser Gly Ile Leu Leu Tyr Lys
1185                1190                1195                120
Gly Asp Lys Asp His Ile Ala Val Glu Leu Tyr Arg Gly Arg Val Arg
                1205                1210                1215
Ala Ser Tyr Asp Thr Gly Ser His Pro Ala Ser Ala Ile Tyr Ser Val
            1220                1225                1230
Glu Thr Ile Asn Asp Gly Asn Phe His Ile Val Glu Leu Leu Thr Leu
        1235                1240                1245
Asp Ser Ser Leu Ser Leu Ser Val Asp Gly Gly Ser Pro Lys Ile Ile
    1250                1255                1260
Thr Asn Leu Ser Lys Gln Ser Thr Leu Asn Phe Asp Ser Pro Leu Tyr
1265                1270                1275                128
Val Gly Gly Met Pro Gly Lys Asn Asn Val Ala Ser Leu Arg Gln Ala
                1285                1290                1295
Pro Gly Gln Asn Gly Thr Ser Phe His Gly Cys Ile Arg Asn Leu Tyr
            1300                1305                1310
Ile Asn Ser Glu Leu Gln Asp Phe Arg Lys Val Pro Met Gln Thr Gly
        1315                1320                1325
Ile Leu Pro Gly Cys Glu Pro Cys His Lys Lys Val Cys Ala His Gly
    1330                1335                1340
Thr Cys Gln Pro Ser Ser Gln Ser Gly Phe Thr Cys Glu Cys Glu Glu
1345                1350                1355                136
Gly Trp Met Gly Pro Leu Cys Asp Gln Arg Thr Asn Asp Pro Cys Leu
                1365                1370                1375
Gly Asn Lys Cys Val His Gly Thr Cys Leu Pro Ile Asn Ala Phe Ser
            1380                1385                1390
Tyr Ser Cys Lys Cys Leu Glu Gly His Gly Gly Val Leu Cys Asp Glu
        1395                1400                1405
Glu Glu Asp Leu Phe Asn Pro Cys Gln Val Ile Lys Cys Lys His Gly
    1410                1415                1420
Lys Cys Arg Leu Ser Gly Leu Gly Gln Pro Tyr Cys Glu Cys Ser Ser
1425                1430                1435                144
Gly Phe Thr Gly Asp Ser Cys Asp Arg Glu Ile Ser Cys Arg Gly Glu
                1445                1450                1455
Arg Ile Arg Asp Tyr Tyr Gln Lys Gln Gln Gly Tyr Ala Ala Cys Gln
            1460                1465                1470
Thr Thr Lys Lys Val Ser Arg Leu Glu Cys Arg Gly Gly Cys Ala Gly
        1475                1480                1485
Gly Gln Cys Cys Gly Pro Leu Arg Ser Lys Arg Arg Lys Tyr Ser Phe
    1490                1495                1500
Glu Cys Thr Asp Gly Ser Ser Phe Val Asp Glu Val Glu Lys Val Val
1505                1510                1515                152
Lys Cys Gly Cys Thr Arg Cys Ala Ser
                1525
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<210> 397
<211> 8
<212> PRT
<213> Mouse

<400> 397
Trp Tyr Asn Ala Trp Asn Glu Lys
1 5

<210> 398
<211> 7
<212> PRT
<213> Mouse

<400> 398
Met Val Ile Ile Thr Thr Lys
1 5

<210> 399
<211> 2206
<212> DNA
<213> Rat

<400> 399
gtttcgtctt aacgccctct ctgcgttggc agaactggcc gtgggctccc gctggtacca 60
tggaacatct cagcccacac agactaagcg gagactgatg ttggtggcgt tcctcggagc 120
atccgcggtg actgcaagta ccggtctcct gtggaagaag gctcacgcag aatctccacc 180
gagcgtcaac agcaagaaga ctgacgctgg agataagggg aagagcaagg acacccggga 240
agtgtccagc catgaaggaa gcgctgcaga cactgcggcc gagccttacc cagaggagaa 300
gaagaagaag cgttctggat tcagagacag aaaagtaatg gagtatgaga ataggatccg 360
agcctactcc acaccagaca aatcttccg gtattttgcc accttgaaag taatcaacga 420
acctggtgaa actgaagtgt tcatgacccc acaggacttt gtgcgctcca taacacccaa 480
tgagaagcag ccagaacact tgggcctgga tcagtacata ataaagcgct tcgatggaaa 540
gaaaattgcc caggaacgag aaaagtttgc tgacgaaggc agcatcttct ataccccttgg 600
agagtgtgga ctcatctcct tctctgacta catcttcctc acaacggtgc tctccactcc 660
tcagagaaat ttcgaaattg ccttcaagat gtttgacttg aatggagatg gagaagtaga 720
catggaggag tttgagcagg ttcaaagcat cattcgctcc cagaccagca tgggcatgcg 780
tcacagagat cgtccaacta ctgggaacac cctcaagtct ggcttatgtt cggccctcac 840
gacctacttt tttggagctg atctcaaagg gaaactgacc attaaaaact tcctggaatt 900
tcagcgtaaa ctgcagcatg acgttctaaa gctggagttt gaacgccatg acccggtaga 960
cgggagaatc tctgagaggc agttcggtgg catgctgctg gcctacagtg gagtgcagtc 1020
caagaagctg accgccatgc agaggcagct gaagaagcac ttcaaggatg ggaagggcct 1080
gactttccag gaggtggaga acttcttcac tttcctgaag aacattaatg acgtggacac 1140
tgcgttaagc ttttaccaca tggctggagc atccctcgat aaagtgacca tgcagcaagt 1200
ggccaggaca gtggcgaaag tcgagctgtc ggaccacgtg tgtgacgtgg tgtttgcact 1260
ctttgactgc gacggcaatg gggagctgag caataaggag tttgtctcca tcatgaagca 1320
gcggctgatg agaggcctgg agaagcccaa ggacatgggc tttacccgtc tcatgcaggc 1380
catgtggaaa tgtgcccaag aaaccgcctg ggactttgct ctacccaaat agtaccccac 1440
ctcctgcacc ttagcacccc gcaatcctgg agtggccttc atgctgctga tgcttctggg 1500
agtagtgccc acatccccat ctttctggaa gtgacctctg gcctcagctg gctgacctct 1560
ccatcctccc ctgacccagt cagtgttccg ctaggctctg aatctgcagt cagatcaaag 1620
gtctaagaca ggaacaagtc ttcaaagcag agaccatagc tcccttaacc agtgccccgt 1680
gggtaaatgc ggggagccct cccacactgg cagccccagg aggcatctct gcagtctctc 1740
actgtggatt taagtaacac aaacgtccct gccatcttcc tcccactgtt ttaaagctgc 1800
aagtttggaa atactctggc aggcaaaggg aagtctgtga tgaacggtaa tgcagatgac 1860
cctggtaccc tgatctggca gggcacctgg tcaggggaag ggtctgcgtc agacaccagc 1920
ggcaccagga aggctctttg ccaccagcac agctcccgat tcaaagtcgc tgctttgagc 1980
ggctctccag aacctcctgc tctttttttt ttcctcccgg ctccctgcga tgcctcctct 2040
gggactctgc ttcactagag ccagggctga gcccctgttc cttgtgtctt gtcccctctc 2100
tatagacctg cagagcgcag ctcagagcct atctgccctc tgtctaatac actcgtaaat 2160
atcactttaa ttatagcact ttgcaggaaa taccccaaaa aaaaaa 2206

<210> 400
<211> 160
<212> DNA
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ccttccatgc ggaaaccaaa gcagcggccg cggccggagc cctcatcat ccccaccaag     180
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cgctctcccg tgcgccttgc tgaccacccc tctgagcgga gctttgagcc cccccсttac    300
acaccacccc ccattctcag ccccgtccgg gaaggctctg gcctctactt caatgccatc    360
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Val Ser Ser His Glu Gly Ser Ala Ala Asp Thr Ala Ala Glu Pro Tyr
    50                  55                  60
Pro Glu Glu Lys Lys Lys Lys Arg Ser Gly Phe Arg Asp Arg Lys Val
65                  70                  75                  80
Met Glu Tyr Glu Asn Arg Ile Arg Ala Tyr Ser Thr Pro Asp Lys Ile
                85                  90                  95
Phe Arg Tyr Phe Ala Thr Leu Lys Val Ile Asn Glu Pro Gly Glu Thr
            100                 105                 110
Glu Val Phe Met Thr Pro Gln Asp Phe Val Arg Ser Ile Thr Pro Asn
        115                 120                 125
Glu Lys Gln Pro Glu His Leu Gly Leu Asp Gln Tyr Ile Ile Lys Arg
    130                 135                 140
Phe Asp Gly Lys Lys Ile Ala Gln Glu Arg Glu Lys Phe Ala Asp Glu
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Gly Ser Ile Phe Tyr Thr Leu Gly Glu Cys Gly Leu Ile Ser Phe Ser
                165                 170                 175
Asp Tyr Ile Phe Leu Thr Thr Val Leu Ser Thr Pro Gln Arg Asn Phe
            180                 185                 190
Glu Ile Ala Phe Lys Met Phe Asp Leu Asn Gly Asp Gly Glu Val Asp
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Met Glu Glu Phe Glu Gln Val Gln Ser Ile Ile Arg Ser Gln Thr Ser
    210                 215                 220
Met Gly Met Arg His Arg Asp Arg Pro Thr Thr Gly Asn Thr Leu Lys
225                 230                 235                 240
Ser Gly Leu Cys Ser Ala Leu Thr Thr Tyr Phe Phe Gly Ala Asp Leu
                245                 250                 255
Lys Gly Lys Leu Thr Ile Lys Asn Phe Leu Glu Phe Gln Arg Lys Leu
            260                 265                 270
Gln His Asp Val Leu Lys Leu Glu Phe Glu Arg His Asp Pro Val Asp
        275                 280                 285
Gly Arg Ile Ser Glu Arg Gln Phe Gly Gly Met Leu Leu Ala Tyr Ser
    290                 295                 300
Gly Val Gln Ser Lys Lys Leu Thr Ala Met Gln Arg Gln Leu Lys Lys
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His Phe Lys Asp Gly Lys Gly Leu Thr Phe Gln Glu Val Glu Asn Phe
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Phe Thr Phe Leu Lys Asn Ile Asn Asp Val Asp Thr Ala Leu Ser Phe
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Tyr His Met Ala Gly Ala Ser Leu Asp Lys Val Thr Met Gln Gln Val
        355                 360                 365
Ala Arg Thr Val Ala Lys Val Glu Leu Ser Asp His Val Cys Asp Val
    370                 375                 380
Val Phe Ala Leu Phe Asp Cys Asp Gly Asn Gly Glu Leu Ser Asn Lys
385                 390                 395                 400
Glu Phe Val Ser Ile Met Lys Gln Arg Leu Met Arg Gly Leu Glu Lys
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Glu Gly Ser Thr Met
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<210> 408
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    50                  55                  60
Val Pro Phe Thr Glu Lys Asp Phe Glu Asn Gly Pro Gln Asn Ile Tyr
65                  70                  75                  80
Asn Leu Tyr Glu Gln Val Ser Tyr Asn Cys Phe Ile Ala Ala Gly Leu
                85                  90                  95
Tyr Leu Leu Leu Gly Gly Phe Ser Phe Cys Gln Val Arg Leu Asn Lys
            100                 105                 110
Arg Lys Glu Tyr Met Val Arg
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      <211> 590
      <212> PRT
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            20                  25                  30
Gly Phe Gly Gln Val Tyr Lys Val Arg His Val His Trp Lys Thr Trp
        35                  40                  45
Leu Ala Ile Lys Cys Ser Pro Ser Leu His Val Asp Asp Arg Glu Arg
    50                  55                  60
Met Glu Leu Leu Glu Glu Ala Lys Lys Met Glu Met Ala Lys Phe Arg
65                  70                  75                  80
Tyr Ile Leu Pro Val Tyr Gly Ile Cys Gln Glu Pro Val Gly Leu Val
                85                  90                  95
Met Glu Tyr Met Glu Thr Gly Ser Leu Glu Lys Leu Leu Ala Ser Glu
            100                 105                 110
Pro Leu Pro Trp Asp Leu Arg Phe Arg Ile Val His Glu Thr Ala Val
        115                 120                 125
Gly Met Asn Phe Leu His Cys Met Ser Pro Pro Leu Leu His Leu Asp
    130                 135                 140
Leu Lys Pro Ala Asn Ile Leu Leu Asp Ala His Tyr His Val Lys Ile
145                 150                 155                 160
Ser Asp Phe Gly Leu Ala Lys Cys Asn Gly Met Ser His Ser His Asp
                165                 170                 175
Leu Ser Met Asp Gly Leu Phe Gly Thr Ile Ala Tyr Leu Pro Pro Glu
            180                 185                 190
Arg Ile Arg Glu Lys Ser Arg Leu Phe Asp Thr Lys His Asp Val Tyr
        195                 200                 205
Ser Phe Ala Ile Val Ile Trp Gly Val Leu Thr Gln Lys Lys Pro Phe
    210                 215                 220
Ala Asp Glu Lys Asn Ile Leu His Ile Met Met Lys Val Val Lys Gly
225                 230                 235                 240
His Arg Pro Glu Leu Pro Pro Ile Cys Arg Pro Arg Pro Arg Ala Cys
                245                 250                 255
Ala Ser Leu Ile Gly Ile Met Gln Arg Cys Trp His Ala Asp Pro Gln
            260                 265                 270
Val Arg Pro Thr Phe Gln Glu Ile Thr Ser Glu Thr Glu Asp Leu Cys
        275                 280                 285
Glu Lys Pro Asp Glu Glu Val Lys Asp Leu Ala His Glu Pro Gly Glu
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Lys Ser Ser Leu Glu Ser Lys Ser Glu Ala Arg Pro Glu Ser Ser Arg
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        355                 360                 365
Ser Ser Gly Lys Arg Leu Ser Gly Val Ser Ser Val Asp Ser Ala Phe
    370                 375                 380
Ser Ser Arg Gly Ser Leu Ser Leu Ser Phe Glu Arg Glu Ala Ser Thr
385                 390                 395                 400
Gly Asp Leu Gly Pro Thr Asp Ile Gln Lys Lys Lys Leu Val Asp Ala
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Ile Ile Ser Gly Asp Thr Ser Arg Leu Met Lys Ile Leu Gln Pro Gln
            420                 425                 430
Asp Val Asp Leu Val Leu Asp Ser Ser Ala Ser Leu Leu His Leu Ala
        435                 440                 445
Val Glu Ala Gly Gln Glu Glu Cys Val Lys Trp Leu Leu Leu Asn Asn
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Ala Asn Pro Asn Leu Thr Asn Arg Lys Gly Ser Thr Pro Leu His Met
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Ala Val Glu Arg Lys Gly Arg Gly Ile Val Glu Leu Leu Leu Ala Arg
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Lys Thr Ser Val Asn Ala Lys Asp Glu Asp Gln Trp Thr Ala Leu His
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Phe Ala Ala Gln Asn Gly Asp Glu Ala Ser Thr Arg Leu Leu Leu Glu
        515                 520                 525
Lys Asn Ala Ser Val Asn Glu Val Asp Phe Glu Gly Arg Thr Pro Met
    530                 535                 540
His Val Ala Cys Gln His Gly Gln Glu Asn Ile Val Arg Thr Leu Leu
545                 550                 555                 560
Arg Arg Gly Val Asp Val Gly Leu Gln Gly Lys Asp Ala Trp Leu Pro
                565                 570                 575
Leu His Tyr Ala Ala Trp Gln Gly His Leu Pro Ile Gly Lys
            580                 585                 590
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INTERNATIONAL SEARCH REPORT

International application No.
PCT/NZ 99/00051

A. CLASSIFICATION OF SUBJECT MATTER

Int Cl[6]: C12N 15/12, 15/18, 15/19

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
C12N 15/12, 15/18, 15/19

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
GenBank, GenBank (ESTs), EMBL, EMBL (ESTs), SwissProt, TREMBL, PIR.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	GenBank (ESTs) Accession no AI412233	SEQ ID NO 119 Claims 1-17, 19, 21, 23, 25, 27, 28
X	GenBank (ESTs) Accession noAA850731	SEQ ID NO 119 Claims 1-17, 19, 21, 23, 25, 27, 28
X	GenBank (ESTs) Accession no AI299847	SEQ ID NO 119 Claims 1-17, 19, 21, 23, 25, 27, 28

[X] Further documents are listed in the continuation of Box C

[ ] See patent family annex

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
8 September 199	15 SEP 1999

Name and mailing address of the ISA/AU	Authorized officer
AUSTRALIAN PATENT OFFICE PO BOX 200 WODEN ACT 2606 AUSTRALIA Facsimile No.: (02) 6285 3929	**GILLIAN ALLEN** Telephone No.: (02) 6283 2266

INTERNATIONAL SEARCH REPORT

International application No.
PCT/NZ 99/00051

Box 1 Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
   because they relate to subject matter not required to be searched by this Authority, namely:

2. ☒ Claims Nos.:1-28
   because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

It is not economically feasible to carry out a full search on all sequences of the claims. Search has been limited to sequences from each of the Examples, namely: -
SEQ ID NOs 68, 118 and 196 from Example 3; SEQ ID NOs 119 and 197 from Example 5; SEQ ID NOs 263, 270 and 344 from Example 5; SEQ ID NOs 273 and 347 from Example 6; SEQ ID NO 129 from Example 7

3. ☐ Claims Nos.:
   because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a)

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest ☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/NZ 99/00051

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	GenBank (ESTs) Accession noW97325	SEQ ID NO 263 Claim nos 1-9, 11, 13, 16, 17, 19, 21, 22-28
X	GenBank (ESTs) Accession no AA111146	SEQ ID NO 263 Claim nos 1-9, 11, 13, 16, 17, 19, 21, 22-28
X	GenBank (ESTs) Accession no AI037414	SEQ ID NO 263 Claim nos 1-9, 11, 13, 16, 17, 19, 21, 22-28
X	GenBank (ESTs) Accession no AI282114	SEQ ID NO 270 Claim nos Claim nos 1-9, 11, 13, 16, 17, 19, 21, 22-28
X	GenBank (ESTs) Accession no AA865643	SEQ ID NO270 Claim nos 1-9, 11, 13, 16, 17, 19, 21, 22-28
X	GenBank (ESTs) Accession no AI140104	SEQ ID NO270 Claim nos 1-9, 11, 13, 16, 17, 19, 21, 22-28
X	GenBank (ESTs) Accession no AA726580	SEQ ID NO 273 Claim nos1-9, 11, 17, 19, 21, 23, 25, 27
X	GenBank (ESTs) Accession no AA407924	SEQ ID NO 273 Claim nos1-9, 11, 17, 19, 21, 23, 25, 27
X	GenBank (ESTs) Accession no AA498629	SEQ ID NO 273 Claim nos1-9, 11, 17, 19, 21, 23, 25, 27